Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Proposed Regulatory Decision Document PRDD2004-04

Florasulam
EF-1343 Suspension Concentrate Herbicide

The technical grade active ingredient (TGAI) florasulam and associated end-use product EF-1343 Suspension Concentrate Herbicide for the control of broadleaf weeds in spring wheat, including durum, spring barley and oats (tank-mix only) are eligible for full registration under Section 13 of the Pest Control Products (PCP) Regulations.

These products were granted temporary registration as per Regulatory Note REG2001-12. This Proposed Regulatory Decision Document (PRDD) provides a summary of the data reviewed and the rationale for the proposed regulatory decision regarding the use of florasulam for control of broadleaf weeds in spring wheat, including durum, spring barley and oats (tank-mix only). The Pest Management Regulatory Agency (PMRA) will accept written comments on the proposal up to 45 days from the date of publication of this document. Please forward all comments to the Publications Coordinator at the address below.

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Foreword

The submission for full registration of florasulam and the end-use product EF-1343 Suspension Concentrate Herbicide, developed by Dow AgroSciences Canada, Inc., for the control of broadleaf weed control in spring wheat, including durum, spring barley and oats (when applied in a tank-mix only), has been reviewed by Health Canada's PMRA.

The PMRA has carried out an assessment of available information in accordance with Section 9 of the PCP Regulations and has found it sufficient pursuant Section 18(b), to allow a determination of the safety, merit and value of florasulam and the end-use product EF-1343 Suspension Concentrate Herbicide. The Agency has concluded that the use of the active ingredient florasulam and the end-use product EF-1343 Suspension Concentrate Herbicide in accordance with the label has merit and value consistent with section 18(c) of the PCP Regulations and does not entail an unacceptable risk of harm pursuant to Section 18(d). Therefore, based on the considerations outlined above, the use of florasulam, the associated manufacturing use products, EF-1440 Manufacturing Concentrate and EF-1343 Manufacturing Concentrate, and the end-use product EF-1343 Suspension Concentrate Herbicide, is proposed for full registration, pursuant to Section 13 of the PCP Regulations.

Methods for analyzing florasulam in environmental media are available to research and monitoring agencies upon request to the PMRA.

A summary of the Agency's findings in support of this decision is found in this PRDD. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document to allow interested parties an opportunity to provide input into the proposed registration decision for this product.

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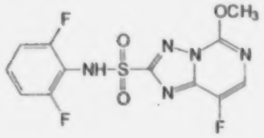
1.0 The active substance, its properties and uses

1.1 Identity of the active substance and impurities

Active substance:	Florasulam
Function:	Herbicide
Chemical names	
IUPAC:	2′,6′,8-trifluoro-5-methoxy-*s*-triazolo[1,5-*c*]pyrimidine-2-sulphonanilide
CAS:	*N*-(2,6-diflurophenyl)-8-fluoro-5-methoxy[1,2,4]triazolo[1,5-*c*]pyrimidine-2-sulfonamide
CAS number:	145701-23-1
Molecular formula:	$C_{12}H_8O_3N_5F_3S$
Molecular weight:	359.3
Structural formula:	
Nominal purity of active:	99.2% nominal (limits: 96.2–100%)
Identity of relevant impurities of toxicological, environmental or other significance:	Based on the raw materials, the manufacturing process used and the chemical structures of the active and impurities, the technical substance is not expected to contain any toxic microcontaminants as identified in Section 2.13.4 of Regulatory Directive DIR98-04, *Chemistry Requirements for the Registration of a Technical Grade of Active Ingredient or an Integrated System Product*, or any Toxic Substances Management Policy (TSMP) Track 1 substances as identified in Appendix II of DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*.

1.2 Physical and chemical properties of active substances and end-use products

Technical product

Property	Result	Comment
Colour and physical state	Off-white	
Odour	Odourless	
Melting point or range	193.5–230.5°C	
Boiling point or range	Not applicable	
Specific gravity	1.53 at 22°C	
Vapour pressure	1×10^{-5} Pa at 25°C	Relatively non-volatile under field conditions
Henry's law constant (K) at 20°C	2.97×10^{-5} Pa m^3 mol^{-1}	Non-volatile from water or moist soil surface
UV–visible spectrum	Medium — λmax Acidic — 259.8 203.8 Basic — 262.4 209.7 Methanolic — 204.1 No absorbance at $\lambda > 300$ nm	Low potential for phototransformation
Solubility in water	Medium — Solubility (g/L) water — 0.121 pH 5 — 0.084 pH 7 — 6.36 pH 9 — 94.2	Soluble at pH 5 and very soluble at pH 7 and pH 9
Solubility in organic solvents	Solvent — Solubility (g/L) acetone — 123.0 acetonitrile — 72.1 ethyl acetate — 15.9 methanol — 9.81 dichloromethane — 3.75 xylene — 0.227 *n*-octanol — 0.184 *n*-heptane — 0.000019	

Property	Result	Comment
n-octanol–water partition coefficient	pH log K_{ow} 4 1.00 7 −1.22 10 −2.06	Bioconcentration is unlikely. Below TSMP cut-off criterion of 5.0
Dissociation constant	$pK_a = 4.54$	Neutral molecule will predominate at pH > 4.54. Adsorption will decrease as pH increases.
Stability (temperature, metals)	No degradation at elevated temperature or in the presence of metals (copper, brass and stainless steel) or metal ions [cuprous, nickel (II), ferric ions] was noted.	

1.3 End-use products: EF-1440 Manufacturing Concentrate
EF-1343 Manufacturing Concentrate
EF-1343 Suspension Concentrate Herbicide

Property	EF-1440 Manufacturing Concentrate	EF-1343 Manufacturing Concentrate	EF-1343 Suspension Concentrate
Colour	Off-white	White, opaque	
Odour	Musty	No discernible odour	
Physical state	Viscous liquid	Liquid	
Formulation type	Manufacturing concentrate	Suspension concentrate	
Guarantee	45% (limits: 43.65–46.35%)	4.84% (limits: 4.60–5.08%)	50 g/L (limits: 47.5–52.4 g/L) or 4.84% (4.6–5.08%)
Container material and description	25 L HPDE drum	HDPE bottle	Cylindrical, injection stretch-blown moulded PET bottle: 1 L
Specific gravity	1.23	1.0318	

1.2 Physical and chemical properties of active substances and end-use products

Technical product

Property	Result	Comment
Colour and physical state	Off-white	
Odour	Odourless	
Melting point or range	193.5–230.5°C	
Boiling point or range	Not applicable	
Specific gravity	1.53 at 22°C	
Vapour pressure	1×10^{-5} Pa at 25°C	Relatively non-volatile under field conditions
Henry's law constant (*K*) at 20°C	2.97×10^{-5} Pa m^3 mol^{-1}	Non-volatile from water or moist soil surface
UV–visible spectrum	Medium λmax Acidic 259.8 203.8 Basic 262.4 209.7 Methanolic 204.1 No absorbance at λ > 300 nm	Low potential for phototransformation
Solubility in water	Medium Solubility (g/L) water 0.121 pH 5 0.084 pH 7 6.36 pH 9 94.2	Soluble at pH 5 and very soluble at pH 7 and pH 9
Solubility in organic solvents	Solvent Solubility (g/L) acetone 123.0 acetonitrile 72.1 ethyl acetate 15.9 methanol 9.81 dichloromethane 3.75 xylene 0.227 *n*-octanol 0.184 *n*-heptane 0.000019	

Property	Result	Comment
n-octanol–water partition coefficient	pH — $\log K_{ow}$ 4 — 1.00 7 — −1.22 10 — −2.06	Bioconcentration is unlikely. Below TSMP cut-off criterion of 5.0
Dissociation constant	$pK_a = 4.54$	Neutral molecule will predominate at pH > 4.54. Adsorption will decrease as pH increases.
Stability (temperature, metals)	No degradation at elevated temperature or in the presence of metals (copper, brass and stainless steel) or metal ions [cuprous, nickel (II), ferric ions] was noted.	

1.3 End-use products: EF-1440 Manufacturing Concentrate EF-1343 Manufacturing Concentrate EF-1343 Suspension Concentrate Herbicide

Property	EF-1440 Manufacturing Concentrate	EF-1343 Manufacturing Concentrate	EF-1343 Suspension Concentrate
Colour	Off-white	White, opaque	
Odour	Musty	No discernible odour	
Physical state	Viscous liquid	Liquid	
Formulation type	Manufacturing concentrate	Suspension concentrate	
Guarantee	45% (limits: 43.65–46.35%)	4.84% (limits: 4.60–5.08%)	50 g/L (limits: 47.5–52.4 g/L) or 4.84% (4.6–5.08%)
Container material and description	25 L HPDE drum	HDPE bottle	Cylindrical, injection stretch-blown moulded PET bottle: 1 L
Specific gravity	1.23	1.0318	

Property	EF-1440 Manufacturing Concentrate	EF-1343 Manufacturing Concentrate	EF-1343 Suspension Concentrate
pH of 1% dispersion in water	4.99	4.36	
Oxidizing or reducing action	No redox reaction	Reacted with K_2MnO_4 solution (by colour change from purple to brown). Non-reactive towards $(NH_4)H_2PO_4$, zinc dust and water.	
Storage stability	4% decrease in active ingredient content after 12 months at ambient temperatures in 25 L HDPE containers	Stable in HDPE and PET bottles after 24 months at ambient temperatures.	
Explodability	Not explosive	Not explosive	

1.3 Details of use

EF-1343 Suspension Concentrate Herbicide is proposed for use on spring wheat, including durum, spring barley and oats (in tank-mix only) at a rate of 100 mL/ha of product (5 g a.i./ha). Accordingly, the product is to be used only in the prairie provinces and the Peace River region of British Columbia, which are the major cereal production areas of Canada. Applied alone, EF-1343 is to be mixed with Agral 90 at 0.2% v/v. Broadleaf weeds listed for control by EF-1343 applied alone include the following:

- volunteer canola (*Brassica napus*) (including Roundup Ready and Liberty Link);
- common chickweed (*Stellaria media*);
- cleavers (*Galium aparine*);
- shepherd's purse (*Capsella bursa pastoris*);
- smartweed (*Polygonum persicaria*);
- stinkweed (*Thlaspi arvense*);
- wild buckwheat (*Polygonum convolvulus*); and
- wild mustard (*Sinapis arvensis*).

Weeds listed for suppression are the following:

- hempnettle (*Galeopsis tetrahit*);
- redroot pigweed (*Amaranthus retroflexus*);
- annual sowthistle (*Sonchus oleraceus*); and
- perennial sowthistle (*Sonchus arvensis*).

EF-1343 is proposed for use as a single application per season, applied by ground equipment only, in a water volume of 50–100 L/ha on cereals from the 2-leaf stage up to and including the flag leaf extended stage. Weeds should be in the 2- to 4-leaf stage at the time of application. EF-1343 Suspension Concentrate Herbicide is proposed for two-way

Property	EF-1440 Manufacturing Concentrate	EF-1343 Manufacturing Concentrate	EF-1343 Suspension Concentrate
pH of 1% dispersion in water	4.99	4.36	
Oxidizing or reducing action	No redox reaction	Reacted with K_2MnO_4 solution (by colour change from purple to brown). Non-reactive towards $(NH_4)H_2PO_4$, zinc dust and water.	
Storage stability	4% decrease in active ingredient content after 12 months at ambient temperatures in 25 L HDPE containers	Stable in HDPE and PET bottles after 24 months at ambient temperatures.	
Explodability	Not explosive	Not explosive	

1.3 Details of use

EF-1343 Suspension Concentrate Herbicide is proposed for use on spring wheat, including durum, spring barley and oats (in tank-mix only) at a rate of 100 mL/ha of product (5 g a.i./ha). Accordingly, the product is to be used only in the prairie provinces and the Peace River region of British Columbia, which are the major cereal production areas of Canada. Applied alone, EF-1343 is to be mixed with Agral 90 at 0.2% v/v. Broadleaf weeds listed for control by EF-1343 applied alone include the following:

- volunteer canola (*Brassica napus*) (including Roundup Ready and Liberty Link);
- common chickweed (*Stellaria media*);
- cleavers (*Galium aparine*);
- shepherd's purse (*Capsella bursa pastoris*);
- smartweed (*Polygonum persicaria*);
- stinkweed (*Thlaspi arvense*);
- wild buckwheat (*Polygonum convolvulus*); and
- wild mustard (*Sinapis arvensis*).

Weeds listed for suppression are the following:

- hempnettle (*Galeopsis tetrahit*);
- redroot pigweed (*Amaranthus retroflexus*);
- annual sowthistle (*Sonchus oleraceus*); and
- perennial sowthistle (*Sonchus arvensis*).

EF-1343 is proposed for use as a single application per season, applied by ground equipment only, in a water volume of 50–100 L/ha on cereals from the 2-leaf stage up to and including the flag leaf extended stage. Weeds should be in the 2- to 4-leaf stage at the time of application. EF-1343 Suspension Concentrate Herbicide is proposed for two-way tank-mix applications with MCPA LV 500 and Curtail M Herbicide. In addition, tank-mixes to extend weed control to include control of certain annual grass species are proposed by adding one of the following products to either the MCPA LV 500 or Curtail M tank-mixes: Assert 300 SC Herbicide; Horizon Herbicide; or Puma Super Herbicide.

2.0 Methods of analysis

2.1 Methods for analysis of the active substance as manufactured

Two reversed phase HPLC/UV methods were provided for the determination of the active, florasulam, and the major impurities present in the technical product. Based on the validation data and the chromatograms provided, the method was assessed to be sufficiently specific, precise and accurate.

2.2 Method for formulation analysis

A reversed phase HPLC/UV method was provided for the determination of florasulam present in EF-1343 Manufacturing Concentrate and EF-1343 Suspension Concentrate. Based on the validation data and the chromatograms provided, the method was assessed to be specific, precise and accurate for use as an enforcement analytical method.

2.3 Methods for residue analysis

2.3.1 Methods for environmental residue analysis

Two chromatographic methods were submitted for the determination of the parent compound, florasulam (SCD-570) and its major transformation product, 2′,6′,8-trifluoro-5-hydroxy-s-triazolo[1,5-c]pyrimidine-2-sulphonanilide metsulfuron-methyl (5-OH XDE 570) in soil. Based on the validation data and the chromatograms provided, the methods were assessed to be sufficiently sensitive, precise, accurate and specific. The method used for the determination of the parent compound and its major transformation product in soil could be used for sediments.

An HPLC/UV method was provided for the determination of the parent compound and its major hydrolysis product, 2′,6′,8-trifluoro-5-hydroxy-s-triazolo[1,5-c]pyrimidine-2-sulphonanilide metsulfuron-methyl (5-OH XDE-570), in drinking water. Based on the validation data and chromatograms provided, the method was assessed to be sufficiently sensitive, precise, accurate and specific. The applicant requested that the analytical method used to quantify XDE-570 and metabolites in crops (wheat and barley) be extended to other flora. A method in animal matrices was not requested, as the potential for bioaccumulation is low due to the very low log K_{ow} values (–2.32 to 1.00) for both the parent and transformation product at pH 4–9.

2.3.2 Multiresidue methods for residue analysis

Protocols from existing multi-residue methods were not found to be suitable for the determination of florasulam.

2.3.3 Methods of residue analysis for plants and plant products

An immunoassay method was acceptable as a data gathering/screening method for the detection of parent compound and metabolites in crops (wheat, barley and oats). An LC-MS/MS method was also acceptable for data gathering (residues of the parent compound). A confirmatory method (GC-MS) was proposed as the enforcement method, and was found to be acceptable for the determination of florasulam in wheat, barley and oats.

2.3.4 Methods of residue analysis of food of animal origin

No analytical method for animal matrices was required, as there were no detectable residues in feed items in crop field trials, and there is no reasonable expectation that finite residues of florasulam will occur in livestock commodities (DIR98-02, Section 2).

3.0 Impact on human and animal health

3.1 Integrated toxicological summary

Florasulam was rapidly and extensively absorbed, with maximal plasma concentrations being achieved within 0.5–1.0 h. Following single or repeat low-dose administration (10 mg/kg bw), greater than 90% of the administered dose was absorbed. Following single high-dose administration (500 mg/kg bw), greater than 80% of the administered dose was absorbed. Bile absorption accounted for approximately 1% of the administered dose within 24 h. Florasulam was rapidly excreted; within 24 h greater than 90% of the administered dose was excreted in the urine and feces. The major route of excretion was via the urine (greater than 80% of the administered dose). Fecal excretion was slightly higher at the high dose compared with the low dose (approximately 17 vs. 7% of the administered dose). There is little potential for accumulation. The highest residue levels were observed in the skin and carcass; however, less than 0.6% of the administered dose remained in the tissue or carcass at sacrifice (168 h post-dosing). Florasulam was not extensively metabolized; the unchanged parent compound, florasulam (XR-570), accounted for greater than 80% of the administered dose. Two other metabolites were identified as OH-phenyl-XR-570 (approximately 3–10% of the administered dose) and a sulfate conjugate of OH-phenyl-XR-570 (approximately 2–4% of the administered dose).

Technical florasulam has low acute toxicity by the oral, dermal and inhalation routes of exposure; is minimally irritating to the eyes and skin; and is not considered to be a dermal sensitizer. The end-use products (see below) have low acute toxicity by the oral, dermal and inhalation routes of exposure; are minimally irritating to the eyes and non-irritating to the skin; and are not considered to be dermal sensitizers:

- EF-1343 Manufacturing Concentrate Herbicide (4.84% florasulam by weight);
- *EF-1440 Manufacturing Concentrate Herbicide* (45% florasulam by weight); and
- EF-1343 Suspension Concentrate Herbicide (4.84% florasulam by weight).

Florasulam was tested in a battery of in vitro (bacterial and mammalian cell gene mutation assays and mammalian cells chromosomal aberration assay) and in vivo (mouse micronucleus assay) mutagenicity studies. There was no evidence of genotoxicity potential in any of these assays; therefore, the weight of evidence suggests that florasulam was not genotoxic under the conditions of the tests performed.

The subchronic and chronic toxicity of florasulam was investigated in the mouse, rat and dog. A 28-d repeat dose dermal toxicity study was also carried out in rats. In the subchronic and chronic studies, treatment-related findings were observed in the kidney in all species and in the liver and adrenal glands in dogs. In the kidney, hypertrophy of the epithelial cells of the collecting ducts occurred in all species tested.

In the mouse, hypertrophy of the epithelial cells was observed in males at 500 mg/kg bw/d and above and in females at 1000 mg/kg bw/d in the 90-d dietary study and in both sexes at 500 mg/kg bw/d and above in the two-year dietary study. The severity of the hypertrophy increased from very slight following 90-d exposure to slight following 12- and 24-month exposures. In the two-year dietary study, a decreased incidence of age-related tubular degeneration with regeneration was noted in females at 500 mg/kg bw/d and above at 12 months and at 1000 mg/kg bw/d at 24 months. In males, the incidence of age-related tubular degeneration with regeneration was comparable to controls at 12 and 24 months; however, the severity was decreased at 24 months at 500 mg/kg bw/d and above.

In the rat, hypertrophy of the epithelial cells was observed in both sexes at 500 mg/kg bw/d and above in the 90-d dietary study and in males at 250 mg/kg bw/d and above and in females at 125 mg/kg bw/d and above in the two-year dietary study. The hypertrophy appeared to become more pronounced over time from 3 to 24 months. In the 90-d dietary study, hypertrophy of the epithelial cells correlated with urinary acidification (both sexes at 500 mg/kg bw/d and above), decreased urinary specific gravity (males at 1000 mg/kg bw/d) and increased kidney weights (both sexes at 500 mg/kg bw/d and above). In the two-year dietary study, hypertrophy of the epithelial cells correlated with elevated serum bicarbonate levels (males at 500 mg/kg bw/d), urinary acidification (males at 250 mg/kg bw/d and above and in females at 125 mg/kg bw/d and above), reduced urinary specific gravity (males at 500 mg/kg bw/d) and increased kidney weights (males at 250 mg/kg bw/d and above and females at 125 mg/kg bw/d and above). Urine volume was not measured in either the 90-d or 2-year dietary study. In the 90-d dietary study, hypertrophy of the epithelial cells and urinary acidification appeared to be reversible following the 4-week recovery period; however, urinary specific gravity continued to be lower and kidney weights continued to be higher at the high dose.

In the rat 90-d dietary study, other histopathological findings in the kidney included degeneration with regeneration in the descending portion of the proximal tubules (females at 500 mg/kg bw/d and above), which was considered to be typical of acute necrosis with regeneration rather than a 90-d old lesion and multi-focal mineralization in the papilla (females at 800 mg/kg bw/d). These lesions did not appear to be reversible. In the rat two-year dietary study, other histopathological findings in the kidneys included a possible slight decreased incidence of age-related tubular degeneration/regeneration and a decreased severity of spontaneous geriatric renal degeneration (chronic progressive glomerularnephropathy) in males at 250 mg/kg bw/d and above, slight decreased incidence of spontaneous geriatric renal disease in females at 250 mg/kg bw/d and minimal reactive hyperplasia of the transitional epithelium and unilateral necrosis of the papilla in males at 500 mg/kg bw/d. The high-dose males also exhibited decreased proteinuria, which was considered to represent less severe chronic renal disease although the decreased specific gravity suggest that dilution may have also contributed to lower values. Body weight and body-weight gain were significantly lower in males at 1000 mg/kg bw/d and in females at 500 mg/kg bw/d and above in the 90-d dietary study and in males at 500 mg/kg bw/d (highest dose tested [HDT]) and in females at 250 mg/kg bw/d (HDT) in the two-year dietary study. This was associated with concomitant lower food consumption in the high-dose animals in the both 90-d and 2-year dietary study.

In a 28-d repeat-dose dermal toxicity study in rats, there were no treatment-related systemic findings at dose levels up to and including 1000 mg/kg bw/d, the HDT.

In the dog, an increased incidence and severity of hypertrophy of the epithelial cells was observed in both sexes at 50 mg/kg bw/d and above in both the 90-d and 1-year dietary study. There were no treatment-related urinalysis findings in either the 90-d or 1-year dietary study. The severity (slight) of the hypertrophy did not appear to increase with prolonged exposure. In the 90-d dietary study, treatment-related findings associated with the liver included increased alkaline phosphatase (ALP) activity in both sexes at 50 and 100 mg/kg bw/d, increased liver weights in both sexes at 100 mg/kg bw/d and a slight increased incidence or severity of hepatic vacuolation in both sexes at 50 and 100 mg/kg bw/d. Increased liver weights and hepatic vacuolation were not observed in the 1-year dietary study. In the 1-year dietary study, treatment-related findings associated with the liver, included increased alanine aminotransferase (ALAT) and ALP activity as well as decreased serum albumin and protein levels in both sexes at 100 mg/kg bw/d. After the high dose was reduced to 50 mg/kg bw/d (week 15), ALP activity remained elevated and serum albumin and protein levels remained lower in both sexes. In the one-year dietary study, no histopathological findings were evident in the liver. In the one-year dietary study, slight vacuolization of the zona reticularis and zona fasciculata in the adrenal glands was observed in the high-dose males and females; however, in the absence of any associated inflamation, necrosis or other changes, the toxicological significance of this finding was uncertain. The vacuolization was consistent with fatty changes. Body weight, body-weight gain and food consumption were significantly lower in both sexes at 100 mg/kg bw/d and remained lower in the high-dose females after the high dose was reduced in the one-year dietary study. Body weight, body-weight gain and food consumption were unaffected by treatment in the 90-d dietary study.

No evidence of an oncogenicity potential of florasulam was found in the oncogenicity and chronic toxicity studies performed on the mouse or rat. With the exception of a slight increased severity in the hypertrophy of the epithelial cells of the collecting duct in mice and rats, there was no evidence to suggest a significant increase in toxicity with increased duration of exposure in mouse, rat or dog. No significant gender sensitivity was evident in any species.

The primary renal histopathological change associated with dietary exposure to florasulam was hypertrophy of the epithelial cells of the collecting ducts, which was observed in all species tested. With the exception of elevated serum bicarbonate levels in the high-dose males in the rat two-year dietary study, there were no toxicologically relevant clinical chemistry findings (serum creatinine, nitrogen or electrolyte levels) to correlate with urinalysis findings in the rat or with hypertrophy of the epithelial cells in the mouse, rat and dog or to indicate an impairment of renal function in any species tested. There was no significant increased incidence of cellular degeneration or necrosis evident in the kidneys in any species tested. Renal function did not appear to be compromised in any species tested and continued ingestion of the test substance did not result in significant deterioration of renal function nor in the development of renal tumours. Functional abnormalities of the collecting duct manifest primarily as an acidification defect and as impaired concentrating ability.

From the histological and ultrastructural appearance of the hypertrophied cells, the site within the collecting duct where they were present and from urine pH changes, it is likely that the cells affected due to florasulam ingestion were the α-intercalated cells. Hypertrophy of the α-intercalated cells have been reported as a physiological response to several factors affecting acid–base homeostasis, including acute respiratory acidosis and metabolic acidosis. Other potential mechanisms include hypokalemia, altered levels of adrenal mineral corticoids, carbonic anhydrase inhibition and HCO^{3-}/Cl^- exchange in the basolateral membrane. Although data are limited, it was concluded that none of these appeared to be the underlying cause of the changes associated with florasulam ingestion. Florasulam may have acted directly on the α-intercalated cells by some unknown mechanism to cause the hypertrophy along with secondary functional effects. However, the continued ingestion of florasulam did not result in apparent deterioration of renal function or in renal tumours and the hypertrophy and urinary acidification appeared to be reversible.

In the rat, reproduction function, reproductive parameters and litter parameters were not influenced by treatment in the P_1 and P_2 parental animals at any dose levels up to and including 500 mg/kg bw/d (HDT). Parental treatment-related findings included lower body weight, body-weight gain and food consumption (P_2 males as well as P_1 and P_2 females); increased kidney weights (P_2 males as well as P_1 and P_2 females); and hypertrophy of the epithelial cells of the collecting duct (P_1 and P_2 in both sexes) at

500 mg/kg bw/d. Sexual maturation of the external sexual organs was unaffected by treatment in the F_1 male and female weanlings. Body weights at birth between the treatment groups and the controls for both F_1 and F_2 pups were comparable. A transient lower body weight was observed in the F_1 and F_2 male and female pups at 500 mg/kg bw/d on lactation days 4 and 7; by lactation day 14 pup body weight was comparable to controls. The transient lower pup body weight may be secondary to decreased maternal food consumption early in the lactation period. There were no other treatment-related findings in the F_1 or F_2 offspring. On the basis of the parental and offspring no observed adverse effect levels (NOAELs) in the rat two-generation reproductive toxicity study (one litter/generation), there was no indication that neonates were more sensitive than adults to the toxic effects of florasulam.

There was no evidence of developmental toxicity in rats at any dose level up to and including 750 mg/kg bw/d (HDT) and in rabbits at any dose level up to and including 500 mg/kg bw/d (HDT). In the rat developmental study, treatment-related maternal findings included lower body weight, body-weight gain and food consumption and increased kidney weights at 750 mg/kg bw/d. In the rabbit developmental study, there were no treatment-related maternal findings at any dose level up to and including 500 mg/kg bw/d. There was no evidence of any irreversible structural changes in either species; therefore, florasulam was not considered to be teratogenic in rat or rabbit. On the basis of the maternal and developmental NOAELs in the rat and rabbit developmental studies, no increased susceptibility of the fetus to in utero exposure to florasulam was demonstrated in either species.

In rats, there were no significant treatment-related findings in the acute or subchronic neurotoxicity screening studies. As well, there was no evidence of neurotoxicity in the rest of the database. Therefore, florasulam was not considered to be neurotoxic.

3.2 Determination of acceptable daily intake

The most appropriate NOAEL of 5.0 mg/kg bw/d in the one-year dietary study in dogs is recommended as the basis for the acceptable daily intake (ADI). Treatment-related findings at the lowest observed adverse effect level (LOAEL) (next highest dose level) included:

- lower body weight, body-weight gain and food consumption (females);
- increased ALP activity (both sexes) as well as decreased serum albumin and protein levels (both sexes) at 50 mg/kg bw/d;
- increased severity of hypertrophy of the epithelial cells of the collecting ducts as well as slight vacuolization of the zona reticularis and zona fasciculata in the adrenal glands in both sexes at initially at 100 mg/kg bw/d, then reduced to 50 mg/kg bw/d.

A safety factor of 100 to account for intra- and inter-species variations was applied to this NOAEL to determine the ADI. No additional safety factor is required.

ADI calculation

$$\text{ADI} = \frac{\text{NOAEL}}{\text{safety factor}} = \frac{5.0\ \text{mg/kg bw/d}}{100} = 0.05\ \text{mg/kg bw/d}$$

3.3 Acute reference dose

An acute reference dose (ARfD) was not established since florasulam was considered unlikely to present an acute hazard. There were no significant treatment-related findings in the acute, short-term, two-generation reproduction or developmental toxicity studies or in the acute or subchronic neurotoxicity studies to indicate a concern for acute dietary risk.

3.4 Toxicological end point selection: occupational and bystander risk assessment

Technical florasulam is of low acute toxicity by the oral, dermal and inhalation routes of exposure; is minimally irritating to the eyes and skin; and is not considered to be dermal sensitizer. The end-use products, EF-1343 Manufacturing Concentrate Herbicide, EF-1440 Manufacturing Concentrate Herbicide and EF-1343 Suspension Concentrate Herbicide, have low acute toxicity by the oral, dermal and inhalation routes of exposure; they are non-irritating to the skin and minimally irritating to the eyes; and are not considered to be dermal sensitizers.

Florasulam was rapidly and extensively absorbed, with maximal plasma concentrations being achieved within 0.5–1.0 h. Florasulam was rapidly excreted, with >90% of the administered dose excreted within 24 h. The major route of excretion was via the urine. There is little potential for accumulation. Florasulam was not extensively metabolized; the unchanged parent compound, florasulam (XR-570), accounted for >80% of the administered dose. Two other metabolites were identified as OH-phenyl-XR-570 (≈3–10% of the administered dose) and a sulfate conjugate of OH-phenyl-XR-570 (≈2–4% of the administered dose).

In subchronic and chronic dietary studies, treatment-related findings were observed in the kidneys in mice, rats and dogs and in the liver and adrenal glands in the dog. In the kidney, hypertrophy of the epithelial cells of the collecting duct was observed in all species tested. In rats, hypertrophy of the epithelial cells correlated with elevated serum bicarbonate levels, urinary acidification, decreased urinary specific gravity and increased kidney weights. In dogs, treatment-related findings associated with the liver included increased ALP activity; decreased serum albumin and protein levels; increased liver weights; and increased incidence or severity of hepatic vacuolation. Dogs also exhibited slight vacuolization of the zona reticularis and zona fasciculata in the adrenal glands; however, in the absence of any associated inflammation, necrosis or other changes, the toxicological significance is uncertain. The most appropriate NOAEL for subchronic and chronic toxicity end points is 5.0 mg/kg bw/d in the 90-d and 1-year dietary studies in dogs. At the LOAEL, 50 mg/kg bw/d, treatment-related findings were observed in the kidneys and liver in the 90-d and 1-year dietary studies and in the adrenal glands in the 1-year dietary study.

Florasulam was not carcinogenic, genotoxic or neurotoxic. With the exception of a slight increased severity in the hypertrophy of the epithelial cells of the collecting duct in mice and rats, there was no evidence to suggest a significant increase in toxicity with increased duration of exposure in mouse, rat or dog. No significant gender sensitivity was evident in any species.

Florasulam is not a developmental or reproductive toxicant. There was no indication from the two-generation reproductive toxicity study (one litter per generation) that neonates were more sensitive than adults to the toxic effects of florasulam. No increased susceptibility of the fetus to in utero exposure to florasulam was demonstrated in rats and rabbits. There was no evidence of teratogenicity in the rat or rabbit developmental studies.

Given the potential for short-term exposure for farmers and intermediate-term exposure for custom applicators, and the predominantly dermal exposure route, a short-term repeat-dose dermal toxicity study is considered to be the most relevant to use in the occupational risk assessment. In a 4-week dermal toxicity study in rat, there were no treatment-related systemic findings in either sex. Local irritation findings included slight transient erythema and edema at the application site in males at 1000 mg/kg bw/d. The LOAEL for systemic toxicity was not determined. The NOAEL for systemic toxicity was 1000 mg/kg bw/d, the HDT.

For the identified toxicity end points, a safety factor of 100 to account for intra- and inter-species variation is considered to be adequate for operator exposure.

3.5 Impact on human and animal health arising from exposure to the active substance or to its impurities

3.5.1 Operator exposure assessment

EF-1343 is a selective herbicide for post-emergent control of annual broad-leaved weeds in spring wheat (including durum), spring barley and oats (as a tank-mix only). It is formulated as a suspension in 800 mL plastic bottles for dilution in water with adjuvant and for application by groundboom spray. The label specifies an application rate of 100 mL product/ha (5 g a.i./ha) once per season between the 2-leaf and flag-leaf stages (early growth period).

There is a potential for short-term to intermediate term exposure to custom applicators who mix, load and apply daily, for a period of approximately 3 weeks. For cereal crops, a custom applicator can spray up to 400 ha per day, handling up to 2 kg a.i./d. The personal protective equipment (PPE) specified on the label for all activities includes a single layer consisting of clean clothing with full-length sleeves and pants and chemical-resistant gloves for mixing, loading, clean-up and repair.

3.5.1.1 Dermal absorption

Male Fischer 344 rats (4/dose/time-to-sacrifice) were administered undiluted or diluted EF-1343 formulation to receive 0.009 or 0.53 mg/cm^2 skin of ^{14}C-XDE-570 (10 µL/cm^2) for a 24-h exposure period. The treated skin was washed at 24 h post-dosing and tape-stripped at sacrifice times of 24, 48 or 72 h post-dosing. Urine and feces were collected from 0 to 24, 24 to 48 and 48 to 72 h post-dosing. Tissues samples (blood, liver, kidney as well as treated and untreated skin) and carcass were collected at the time of sacrifice.

In both the low- and high-dose groups, the majority of the applied dose (71–90%) was removed in the skin wash at 24 h post-dosing. In the low-dose groups, a total of 12–22% of the applied dose was found in the urine, feces, metabolism cage washes, tissues, carcass as well as untreated and treated skin residues, the majority of which (99%) was from skin residues. In the high-dose group, a total of 10–11% of the applied dose was found in the urine, feces, tissues, carcass as well as untreated and treated skin, the majority of which (95–99%) was from skin residues. No significant difference or trend was observed in skin residues with time-to-sacrifice.

The PMRA recommends a dermal absorption value of 22%. This estimate is considered conservative based on the observation that the majority of the dose is retained in the treated skin and not considered likely to become systemically available in total, and that the study's exposure period (24 h) is greater than anticipated in the field. Therefore, uptake of the applied dose has been maximized in this study.

3.5.1.2 Exposure assessment

The Pesticide Handlers Exposure Database (PHED) Version 1.1 data provided an adequate basis for estimating operator exposure for the proposed use. The data were based on high confidence PHED runs with PPE similar to that proposed on the label; adequate numbers of replicates; and A and B grade data. The PHED data does not provide exposure estimates for clean-up or repair activities, nor quantify the variability of exposure estimates.

Total daily exposure was estimated for custom application of 2 kg/d of florasulam to 400 ha of cereal crops per day by groundboom (including mixing and loading). For mixing and loading, exposure was estimated from PHED subsets for single layer protection and gloves. For the application, exposure was estimated from PHED subsets for single layer protection without gloves. Exposure estimates were based on best fit statistical analyses. Unit exposure estimates (µg a.i./kg a.i. handled) were based on total dermal and inhalation deposition and adjusted for dermal absorption of 22%.

The primary route of exposure was dermal. Inhalation exposure accounted for 3% of the total deposited dose and 12% of the total absorbed dose. The mixer and loader exposure contributed 61% of the total daily exposure.

For custom applicators mixing, loading and applying 2 kg of active ingredient per day to 400 ha of cereal crops using groundboom equipment and wearing a single layer of protective clothing and gloves during mixing and loading, the total daily exposure was estimated to be 2.48 µg a.i./kg bw/d and the total daily systemic dose was estimated to be 0.6 µg/kg bw/d, based on a dermal absorption value of 22%. Exposure to farmers who mix, load and apply products is expected to be lower than custom applications.

The exposure estimate and margin of exposure (MOE) for custom applicators mixing, loading and applying the product are presented in Table 3.5.1.2.1.

For custom mixers, loaders and applicators (M/L/As), an acceptable MOE of 400 000 was attained based on total exposure (from dermal and inhalation routes of exposure) and the NOAEL of 1000 mg/kg bw/d from the 28-d rat dermal study. A novel toxicity end point (liver effects) was observed in the dog (90-d) and, although the study is more appropriate for exposure of longer duration, an acceptable MOE of 8000 was attained for systemic exposure.

Table 3.5.1.2.1 Exposure estimates and resulting MOEs

Exposure scenario	Daily exposure[a] (mg a.i./kg bw/d)	Toxicity end point (mg/kg bw/d)	MOE
Wheat, barley and oats custom M/L/A	0.0025	28-d dermal: rat NOAEL = 1000	400 000

[a] Sum of M/L/A dermal and inhalation exposures

3.5.2 Bystanders

For the proposed agricultural use scenarios, bystander exposure is considered minimal.

3.5.3 Post-application exposure

Re-entry activities for cereals crops include scouting and mechanical harvesting and involve minimal contact with treated foliage. Post-application exposure is considered minimal.

The primary route of exposure was dermal. Inhalation exposure accounted for 3% of the total deposited dose and 12% of the total absorbed dose. The mixer and loader exposure contributed 61% of the total daily exposure.

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For the proposed agricultural use scenarios, bystander exposure is considered minimal.

3.5.3 Post-application exposure

Re-entry activities for cereals crops include scouting and mechanical harvesting and involve minimal contact with treated foliage. Post-application exposure is considered minimal.

4.0 Residues

4.1 Residue summary

4.1.1 Wheat metabolism

Florasulam (>98%), formulated as a suspension concentrate (EF-1343), was radiolabelled as [^{14}C]-phenyl-XDE-570 or [^{14}C]-TP-XDE-570 and applied once to winter wheat at a rate of 50 g a.i./ha. Separate applications were made to plants at crop growth stage BBCH30 (stem elongation; 'early application') and BBCH49 (postflag leaf emergence/first awns visible; 'late application'). Winter wheat was planted in tubs containing sandy loam soil (10 plants/tub), and tubs were placed outdoors for the duration of the in-life phase of the study. In addition to exposure to precipitation, the plants were watered at the soil surface as required. The test substance was applied until run-off using a spray gun. Immature plants were harvested within 18 hours of treatment (day 0), and at 30 days after treatment; wheat straw, ears, and grain were harvested at crop maturity (129 days after early application and 65 days after late application).

Total radioactive residues (TRRs) in each commodity were determined by combustion/LSC. Immature plant samples (0 and 30 day preharvest intervals [PHIs]), and mature wheat straw (129 or 65 day PHI) from early and late applications were extracted, and residues were characterized or identified by TLC and HPLC with UV detection. Sample analysis was initiated within three days of harvest. The petitioner reported that the chromatographic profiles of fresh samples and samples stored for 6, 8 and 9 months were very similar, and concluded that residues of florasulam in winter wheat are stable for up to 9 months of storage.

The TRRs in the immature plant following the early application (BBCH 30) are summarized in Table 4.1.1.1; whereas the TRRs in the immature plant following the late application (BBCH49) are summarized in Table 4.1.1.2. No further attempts to characterize or identify the residues in ears and grain were made due to the low TRRs in these commodities.

Table 4.1.1.1 TRRs in the immature plant following early application (BBCH30)

Sample	$[^{14}C]$-phenyl-XDE-570	$[^{14}C]$-TP-XDE-570
Immature plant	**0 day PHI**	
	4.1 ppm	3.2 ppm
	30 day PHI	
	0.4 ppm	0.4 ppm
	129 day PHI	
Straw	0.048 ppm	0.073 ppm
Ears	0.003–0.008 ppm	0.003–0.008 ppm
Grain	0.001–0.002 ppm	0.001–0.002 ppm

Table 4.1.1.2 TRRs in the immature plant following late application (BBCH49)

Sample	$[^{14}C]$-phenyl-XDE-570	$[^{14}C]$-TP-XDE-570
Immature plant	**0 day PHI**	
	0.68 ppm	0.76 ppm
	30 day PHI	
	0.12 ppm	0.13 ppm
	65 day PHI	
Straw	0.41 ppm	0.32 ppm
Ears	0.003 ppm	0.003 ppm
Grain	0.002–0.008 ppm	0.002–0.008 ppm

The majority of the radioactivity in the immature wheat plants and the wheat straw from both early and late applications were extracted:

- 94–97% of the TRRs in immature plants at the 0 day PHI;
- 63–78% of the TRRs in immature plants at the 30 day PHI; and
- 59–79% of the TRRs in wheat straw at either the 129 day or 65 day PHI were extractable.

The proportion of extractable radioactivity was similar for early and late application samples, and for PH and TP labels.

In immature plants from both the early and late applications, 90–94% and 51–69% of the TRRs were identified at the 0 and 30 day PHI, respectively. The metabolites identified in the immature wheat samples as well as their quantities are summarized in Table 4.1.1.3.

In wheat straw, however, 44–50% and 9–15% of the TRRs were identified from the late application (65 day PHI) and the early application (129 day PHI), respectively. No parent compound was identified, and no other metabolites were identified at >10% of the TRRs. The metabolites identified in the wheat straw samples as well as their quantities are summarized in Table 4.1.1.4.

Table 4.1.1.3 Metabolites identified in immature wheat

Metabolite	% of TRRs	ppm
0 day PHI		
Parent florasulam (predominant metabolite)	63–84%	0.57–2.9
Glucose conjugate of 4-OH-(phenyl)-florasulam	8.5–25%	0.058–0.80
4-OH-(phenyl)-florasulam	0.4–1.2%	0.003–0.038
2-sulphonamide (TP label only)	0.7–1.5%	0.005–0.051
30 day PHI		
Parent florasulam (predominant metabolite)	27–32%	0.03–0.12
Glucose conjugate of 4-OH-(phenyl)-florasulam	13–42%	0.024–0.083
4-OH-(phenyl)-florasulam	6.8–15.1%	0.027–0.060
2-sulphonamide (TP label only)	0.7–1.5%	0.005–0.051

Table 4.1.1.4 Metabolites identified in wheat straw

Metabolite	% of TRRs	ppm
Late application (65 day PHI)		
Parent florasulam	7–14%	0.02–0.057
4-OH-(phenyl)-florasulam	5.5–14%	0.017–0.059
Glucose conjugate of 4-OH-(phenyl)-florasulam	13–21.5%	0.041–0.088
2-sulphonamide (TP label only)	19%	0.058
Early application (129 day PHI)		
Parent florasulam	None	
4-OH-(phenyl)-florasulam	1.6–8.4%	0.001–0.004
Glucose conjugate of 4-OH-(phenyl)-florasulam		
2-sulphonamide (TP label only)		

Table 4.1.1.1 TRRs in the immature plant following early application (BBCH30)

Sample	[^{14}C]-phenyl-XDE-570	[^{14}C]-TP-XDE-570
Immature plant	**0 day PHI**	
	4.1 ppm	3.2 ppm
	30 day PHI	
	0.4 ppm	0.4 ppm
	129 day PHI	
Straw	0.048 ppm	0.073 ppm
Ears	0.003–0.008 ppm	0.003–0.008 ppm
Grain	0.001–0.002 ppm	0.001–0.002 ppm

Table 4.1.1.2 TRRs in the immature plant following late application (BBCH49)

Sample	[^{14}C]-phenyl-XDE-570	[^{14}C]-TP-XDE-570
Immature plant	**0 day PHI**	
	0.68 ppm	0.76 ppm
	30 day PHI	
	0.12 ppm	0.13 ppm
	65 day PHI	
Straw	0.41 ppm	0.32 ppm
Ears	0.003 ppm	0.003 ppm
Grain	0.002–0.008 ppm	0.002–0.008 ppm

The majority of the radioactivity in the immature wheat plants and the wheat straw from both early and late applications were extracted:

- 94–97% of the TRRs in immature plants at the 0 day PHI;
- 63–78% of the TRRs in immature plants at the 30 day PHI; and
- 59–79% of the TRRs in wheat straw at either the 129 day or 65 day PHI were extractable.

The proportion of extractable radioactivity was similar for early and late application samples, and for PH and TP labels.

In immature plants from both the early and late applications, 90–94% and 51–69% of the TRRs were identified at the 0 and 30 day PHI, respectively. The metabolites identified in the immature wheat samples as well as their quantities are summarized in Table 4.1.1.3.

In wheat straw, however, 44–50% and 9–15% of the TRRs were identified from the late application (65 day PHI) and the early application (129 day PHI), respectively. No parent compound was identified, and no other metabolites were identified at >10% of the TRRs. The metabolites identified in the wheat straw samples as well as their quantities are summarized in Table 4.1.1.4.

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Glucose conjugate of 4-OH-(phenyl)-florasulam	13–42%	0.024–0.083
4-OH-(phenyl)-florasulam	6.8–15.1%	0.027–0.060
2-sulphonamide (TP label only)	0.7–1.5%	0.005–0.051

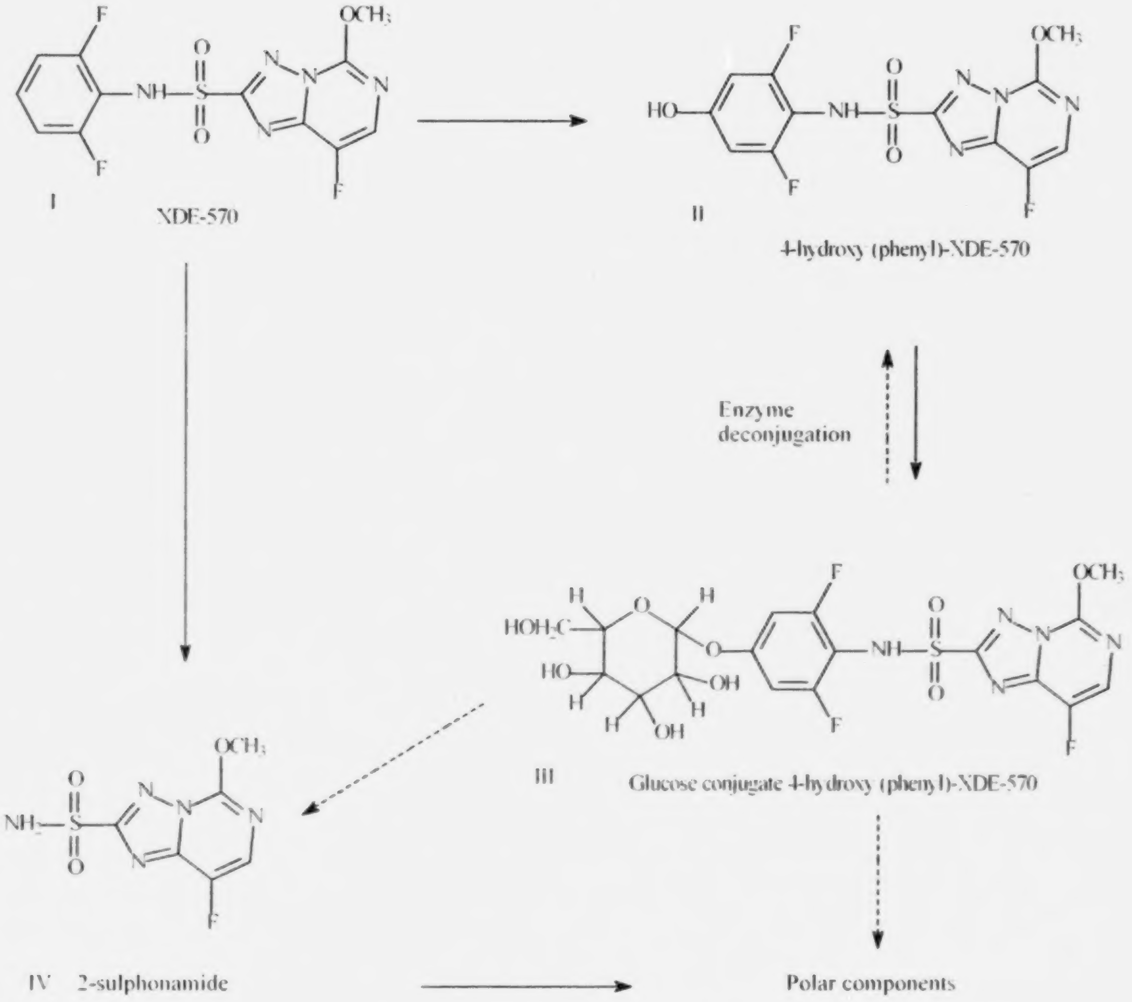
Table 4.1.1.4 Metabolites identified in wheat straw

Metabolite	% of TRRs	ppm
Late application (65 day PHI)		
Parent florasulam	7–14%	0.02–0.057
4-OH-(phenyl)-florasulam	5.5–14%	0.017–0.059
Glucose conjugate of 4-OH-(phenyl)-florasulam	13–21.5%	0.041–0.088
2-sulphonamide (TP label only)	19%	0.058
Early application (129 day PHI)		
Parent florasulam	None	
4-OH-(phenyl)-florasulam	1.6–8.4%	0.001–0.004
Glucose conjugate of 4-OH-(phenyl)-florasulam		
2-sulphonamide (TP label only)		

The unidentified residues in immature wheat plants and wheat straw from both early and late applications consisted of several minor components characterized as being more polar than florasulam (0.3–45.8% of the TRRs; 0.011–0.039 ppm). Each of the components was estimated to be present at less than 0.01 ppm.

In immature wheat plants, higher TRRs were observed following the early application compared to the late application; however, in mature wheat straw, higher residues were observed following the late application. At the 0 day and 30 day PHIs, the majority of the residues in the immature plants were identified, and the predominant residue was the parent florasulam. As the PHI increased, the identified residues and the amount of parent decreased, indicating degradation to minor components. The metabolism of florasulam in wheat proceeds via hydroxylation at the 4-position of the phenyl ring with subsequent glucose conjugation, and by cleavage of the sulphonamide bridge, as indicated by the detection of the metabolites 4-OH-(phenyl)-florasulam, its glucose conjugate and 2-sulphonamide.

Figure 4.1.1.1 Proposed metabolic pathway of florasulam in wheat


I
XDE-570
II
4-hydroxy (phenyl)-XDE-570
Enzyme deconjugation
III
Glucose conjugate 4-hydroxy (phenyl)-XDE-570
IV 2-sulphonamide
Polar components

4.1.2 Poultry metabolism

Florasulam, radiolabelled as either [UL-aniline-^{14}C]XDE-570 (A-label) or [triazolopyrimidine-9- ^{14}C]XDE-570 (TP-label), was administered to two groups of 10 laying hens at a dose level of 0.76 mg/kg bw/day. The dose was administered orally by capsule, twice daily for five consecutive days. The dose was equivalent to a dietary burden of 10.7 ppm florasulam, at an average feed consumption of 0.13 kg/day. Samples of eggs and excreta were collected throughout the study. The hens were sacrificed approximately 24 hours after the final dose and samples of fat, composite muscle (light and dark), skin and liver were collected for analysis.

TRRs in tissue, egg and excreta samples were determined by combustion and liquid scintillation counting (LSC). Extraction and residue characterization/identification by HPLC and TLC were performed on samples of eggs, skin and excreta. Samples and extracts were stored frozen at approximately -20°C during the study. All samples were prepared and characterized within 28 days of sacrifice; therefore, no storage stability tests were necessary.

The majority of the administered radioactivity was recovered in excreta (91.3 and 96.9% for A- and TP-labels, respectively), whereas the total residues in the tissues and eggs accounted for <0.02% of the administered dose. The TRRs in muscle, fat and liver were less than the limits of quantification (LOQ) for those matrices (all $\leq$0.001 ppm). The TRRs in skin were 0.005–0.0066 ppm and in eggs were 0.004 ppm. As the total radioactivity in liver, fat and muscle samples was very low, no further residue characterization was conducted. Greater than 84% of the TRRs were extracted from eggs, skin, and excreta, and the only metabolite identified in those matrices was parent florasulam (79.7–95.1% of the TRRs).

The results obtained with the two different labels indicate that no bridge cleavage occurred. The low tissue burden and high excretion rate of unmetabolized florasulam, as well as the low log K_{ow} (1.00 at pH 4.00 and -1.22 at pH 7.0) indicate a low potential for sequestration in fatty tissues.

4.1.3 Goat metabolism

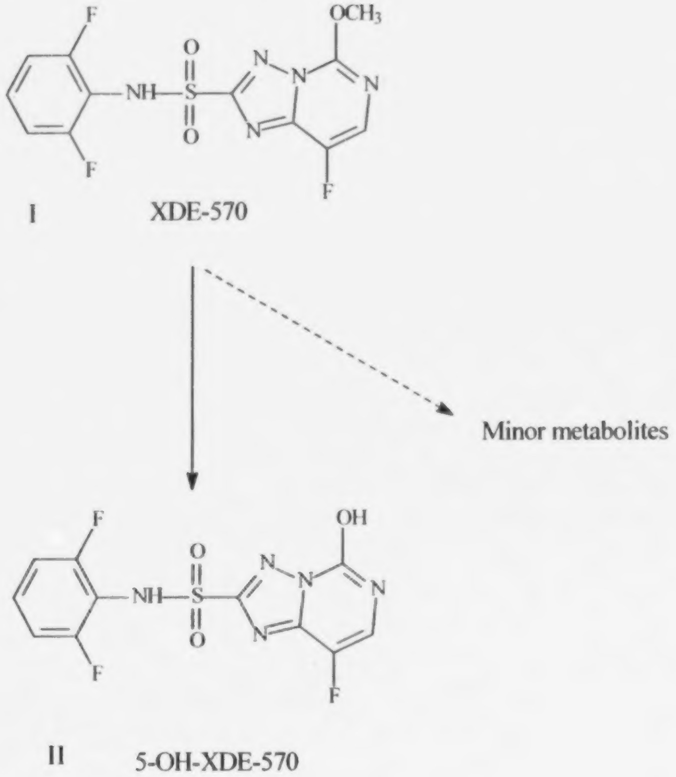
Florasulam, radiolabelled as either [UL-aniline-^{14}C]XDE-570 (A-label) or [triazolopyrimidine-9- ^{14}C]XDE-570 (TP-label), was administered daily to two lactating goats (one per treatment) at a dose level of approximately 0.48 mg/kg bw/day. The dose was administered orally for five consecutive days using a bolus gun and was equivalent to a dietary burden of approximately 11 ppm florasulam at an average feed consumption of 2 kg/day. Samples of milk, urine and feces were collected throughout the study. Approximately 24 hours after the final dose, the animals were sacrificed and samples of tissues (liver, kidney, muscle and fat), blood, gastrointestinal contents and urine from the bladder were collected.

TRRs in tissues, milk and excreta were determined by combustion radioanalysis and/or LSC. Samples of urine, milk, liver and kidney were extracted in order to characterize the residues. Solvent extraction efficiency tests indicated that recovery of spiked radioactivity was 88–104%. Extracts were analyzed by reverse phase HPLC to identify residues, with confirmation by TLC. Samples and extracts were stored frozen at approximately -20°C during the study. All tissue and milk samples were prepared and characterized within 27 days of sacrifice, and urine samples were analyzed within 51 days of sacrifice. Therefore, no storage stability tests were necessary.

Recoveries of the administered dose (AD) were 89% for the A-label and 83% for the TP-label. The majority of the radioactivity was excreted in the urine and feces, accounting for a total of 99.8% of the recovered radioactivity. Residues in milk and tissues each represented <0.1% AD, and totalled 0.123% AD and 0.139% AD for the A- and TP-labels, respectively. The highest concentration of residues in tissues was found in the kidney (0.039–0.069 ppm), followed by liver (0.023–0.033 ppm), milk (0.016–0.033 ppm), fat (0.0016–0.0017 ppm), and muscle (0.0009–0.0016 ppm). Greater than 90% of the TRRs in urine, milk, and kidney were extractable; however only 22.4–23.2% of the TRRs in liver were extracted. Unextractable residues in liver were treated with protease, which released an additional 41.8 and 56.5% of the TRRs (0.0138 and 0.013 ppm) of the A- and TP-labels, respectively. However, 32.5–43.1% of the TRRs (0.0075–0.014 ppm) in liver remained bound, and were not further analyzed. The predominant metabolite identified in all extracts was the parent compound, representing 87.6–98.3% of the TRRs in urine, milk, and kidney, and 15.2–15.3% of the TRRs in liver. A minor metabolite representing up to 1.5% of the TRRs was tentatively identified as 5-OH-florasulam in urine, liver and kidney samples. No other metabolites were identified.

The results obtained with the two different labels indicate that no bridge cleavage occurred. The low tissue burden and high excretion rate of unmetabolized florasulam, as well as the low log K_{ow} (1.00 at pH 4.00 and -1.22 at pH 7.0) indicate a low potential for sequestration in fatty tissues.

Figure 4.1.3.1 **Proposed metabolic pathway of florasulam in animal matrices**



4.1.4 Confined rotational

Florasulam (XDE-570, > 97% a.i.), formulated as a suspension concentrate (E-1343), was radiolabelled either as [UL-phenyl-^{14}C]XDE-570 or [9-triazolopyrimidine-^{14}C]XDE-570 and applied to sandy loam soil at a rate of 7.5 g a.i./ha. The rotational crops (spring wheat, sunflowers, cabbage and carrots) were planted at 30 days after treatment (DAT).

Spring wheat (ears and straw), sunflower (heads and stems), cabbage (shoots) and carrots (leaves and roots) were harvested at maturity: 168 DAT for spring wheat and sunflowers, 195 DAT for cabbage, and 156 DAT for carrots. Crop fractions were subjected to three sequential surface washes (an aqueous wash, a dichloromethane wash and a methanol wash), and each wash was analyzed to determine total ^{14}C-residues (TRRs) using combustion/LSC. None of the fractions had TRRs greater than 0.01 ppm, and therefore, no further attempt was made to characterize/identify residues in rotational crops.

Soil from 0 and 30 DAT was extracted and residues were analyzed by TLC and HPLC. Parent florasulam and 5-OH-florasulam were the only metabolites identified. A soil metabolism study showed that the sorption of florasulam and 5-OH-florasulam increased with time, so residues remaining in soil are less mobile and less bioavailable. Therefore, the concentration of the residues in the soil for potential uptake by secondary crops is very low. The results of the confined crop rotational study support a 30-day plantback interval (PBI) for all crops.

4.1.5 Analytical methods

Analytical method GRM 97.01 (immunoassay [IA] kits) developed by Strategic Diagnostics Inc. (SDI) and Dow AgroSciences was used to determine residues of florasulam in wheat, barely, oats and rye. This method was previously reviewed by the PMRA for the registration of florasulam on wheat, barley and oats and was deemed acceptable for data gathering purposes based on method validation. Residues of florasulam are extracted from matrices using an acidified acetone solution, followed by clean-up on C_{18} SPE columns. Forage and first hay samples are excluded from the C_{18} SPE clean-up columns. These samples are instead partitioned in a dilute acid/hexane solution followed by the addition of a NaOH buffer and dilution. All samples are analyzed using SDI XDE-570 IA kits. An aliquot of diluted extract is transferred to a test tube with enzyme conjugated florasulam and magnetic particles coated with antibodies specific to florasulam. During incubation, the florasulam in the extract competes with the enzyme conjugate for antibody sites on the magnetic particles. The bound material is held in place by a magnetic field while the unbound is decanted from the test tube. An enzyme substrate (hydrogen peroxide) and a chromogen are added to the remaining bound material in order to detect the presence of florasulam. The reaction is stopped by adding an acid. The amount of florasulam present is determined by the colour intensity of the final material. An RPA-1 RaPID Photometric Analyzer is used to measure the absorbance of the sample at 450 nm. The concentration of florasulam in samples is calculated from the regression equation using the preprogrammed software in the Photometric Analyzer. A low concentration of florasulam in the sample will yield a sample with a more intense colour (and vice versa).

Since the immunoassay kits have a high affinity for 4-OH-florasulam and the 4-OH-florasulam glucose conjugate metabolites, the residue results are higher than results from a gas chromatography with mass selective detection (GC-MSD) method. Therefore, any samples with residues greater than LOQ by the IA screening method were also analyzed by method GRM 98.01, a GC-MSD method specific for florasulam. Method GRM 98.01 was also previously evaluated by the PMRA and was deemed acceptable as an enforcement method. In this method, the residues are extracted with an acetone:water:acetic acid (80:20:1) solution. An aliquot of the extract is then filtered on a graphitized carbon solid phase extraction column. The sample is diluted after the acetone has evaporated with 0.01 NHCl and cleaned up using C_{18} SPE columns. The resulting eluent is then extracted with methyl-tert-butyl ether and evaporated to dryness. Derivitization of the sample is done with iodomethane to form the *N*-methyl derivative. The sample is evaporated to dryness and reconstituted in a 5% sodium thiosulfate solution, then partitioned into toluene (containing *N*-propyl-florasulam as an internal standard) prior to analysis by GC-MSD.

The Canadian trials used the LC-MS/MS method GRM 99.17 for analysis (which was not previously evaluated by the PMRA). Residues are extracted from the homogenized grain sample using acetone/water/acetic acid solution. An aliquot of the extract is acidified and extracted again into methyl tertiary butyl ether (MTBE), which was evaporated to dryness and reconstituted in ethyl acetate, then finally purified with a strong anion exchange (PE-AX) SPE column. Residues are eluted with 1% formic acid in water/methanol solution containing *N*-methyl florasulam as an internal standard. The quantitation of residues is performed by LC-MS/MS with a different mobile phase (Solvent A [1:1 ACN:methanol with 0.1% acetic acid], Solvent B [water with 0.1% acetic acid]). Analysis is performed using a YM AM-302-3 column installed in a PE/Sciex API 2000 LC, with a PE/Sciex MSD operating in the positive ion ESI mode. The LOD and LOQ for grain in this study were reported as 0.003 ppm and 0.01 ppm, respectively. Recoveries of florasulam in forage, hay, straw, and grain spiked at LOQ were between 70–120% (±20% SDEV), indicating acceptable repeatability and precision.

4.1.6 Freezer storage stability study

The following ground wheat samples were spiked with florasulam (99.7% a.i.) at 5 µg/mL and stored at -20°C for the following maximum durations (in days):

- immature green plants, immature dried plants (498);
- forage (524);
- grain (410);
- straw (313); and
- hay (459).

A set of 0-day samples and other spiked samples were removed at various time intervals and analyzed to study the stability of florasulam. The analytical methods employed to detect residues were GRM 97.01 (IA) and GRM 98.01 (GC-MSD). Both methods were validated at a level of 0.05 ppm for the wheat (immature green and dried plants, forage, straw and hay) and at a level of 0.01 ppm for wheat grain.

In the spiked immature dried plants, forage, grain, and straw no significant degradation was reported, indicating that residues of florasulam were stable at -20°C for the duration of the study. However, significant degradation was observed in immature green plants (38%) and in hay (31%). A correction factor was necessary for residues in/on hay in the crop field trial, due to in storage dissipation. No correction for immature green plants was made since all residues were below the LOQ using the immunoassay screening method and were not further analyzed. The freezer storage stability data for wheat was extended to barley and oat matrices.

4.1.7 Supervised residue trials

A total of 44 supervised crop field trials were conducted encompassing regions 1, 5, 5A, 5B, 7, 7A, 8, and 14 on wheat, barley, rye, and oat during the 1997 and 2001 growing seasons. At each test location, florasulam (suspension concentrate) was applied once to the crop from tillering to ligule stage using foliar broadcast or backpack sprayers at a target rate of 10 g a.i./ha/season. An adjuvant, Agral 90 (0.2% v/v), was added to the spray mixture for all applications. Wheat, oat, barley and rye were harvested at 7, 15 and 30 days after treatment (DAT) for the American trials, while the Canadian trials were harvested at 54, 58 and 60 DAT.

Both the immunoassay screening method (GRM 97.01) and the GC-MSD confirmatory method (GRM 98.01) were deemed acceptable for data gathering and enforcement methods, respectively. The LC-MS/MS method GRM 99.17 used in the Canadian trials was also deemed acceptable as a data gathering method based on method validation. The reported LOQs for method GRM 97.01 were 0.057 ppm (forage), 0.064 ppm (hay), 0.087 ppm (straw), and 0.017 ppm (grain). The reported LOQ for method GRM 98.01 was 0.05 ppm (forage and hay). The reported LOQ for oat and barley grain from method GRM 99.17 was 0.01 ppm.

The maximum storage intervals (in days) for samples from harvest to analysis were 450 (wheat), 463 (oat), 433 (barley) and 491 (rye). The storage stability data for wheat will be considered adequate to support the storage conditions and intervals of samples from the submitted wheat, barley, oat and rye field trials. Residues in hay samples were corrected for degradation observed during storage (31% in 459 days).

Residues in wheat hay ranged from 0.028–0.071 ppm at a 7 day PHI, and from 0.023–0.058 ppm at a 15 day PHI. Oat hay residues ranged from 0.015–0.054 ppm at a 7 day PHI. Remaining samples of wheat, oat and barley (hay and forage), as well as oat and barley grain were ≤LOQ at various PHIs. Residue decline data show that residues of florasulam decreased by 96.2% in rye forage with increasing PHIs (0 to 15 days).

4.1.8 Processing studies

Residues of florasulam were non quantifiable (<0.01 ppm) in the raw agricultural commodities (grain of wheat, barley and oats) following a single foliar application at an exaggerated rate of 10 g a.i./ha/season. Therefore, no concentration factor was estimated.

4.1.9 Meat/Milk/Poultry/Eggs

Based on data from the ruminant and poultry metabolism studies, in which goats and hens were dosed at levels greater than the maximum theoretical dietary burdens (MTDB) of 0.03 ppm for dairy cattle and 0.01 ppm for beef cattle and poultry, there is no reasonable expectation that finite residues of florasulam will occur in livestock commodities

(DIR98-02, Section 2). Therefore, livestock feeding studies and MRLs for livestock commodities are not required at this time.

4.1.10 Dietary risk assessment

The florasulam chronic dietary exposure assessment was conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 1.3), which incorporates consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intake by Individuals (CSFII), 1994-1996 and 1998. The CSFII data are based on the reported consumption of more than 20 000 individuals over two non-consecutive survey days. Foods "as consumed" (e.g., apple pie) are linked to defined food commodities (e.g. apples, peeled fruit [cooked or fresh]) using publicly available recipe translation files. Consumption data are averaged for the entire population and within population subgroups for chronic exposure assessment, but are retained as individual consumption events for acute exposure assessment. The ADI for florasulam was determined to be 0.05 mg/kg bw/day, based on a NOAEL of 5.0 mg/kg bw/day and a safety factor of 100. The currently proposed uses for florasulam encompass only agricultural use sites. Therefore, when addressing aggregate exposures, only the dietary pathways of food and drinking water were considered. The chronic dietary exposure from all supported florasulam food uses for the representative population subgroups ranged from 0.0% to 0.1% of the ADI. Aggregate exposure from food and water is considered acceptable and below the level of concern.

5.0 Fate and behaviour in the environment

5.1 Physical and chemical properties relevant to the environment

The solubility of florasulam in reagent water at pH of 5, 7 and 9 is 0.084, 6.36 and 94.2 g/L, respectively. Florasulam is soluble at pH 5 and very soluble at pH 7 and 9. The vapour pressure is 1×10^{-5} Pa at 25°C, indicating that florasulam is relatively non-volatile under field conditions. Based on the values for solubility in pure water, vapour pressure and the molecular weight, K is 2.97×10^{-5} Pa m^3 mol^{-1} (or 2.93×10^{-10} atm m^3 mol^{-1}). This value indicates that florasulam is non-volatile from water or moist soil surfaces. The log K_{ow} values are 1.00, –1.22 and –2.06 for pH 4, 7 and 10, respectively, indicating that bioconcentration or bioaccumulation is unlikely. The pK_a is 4.54 ± 0.06. This indicates that the cation will predominate at pH <4.54 and that adsorption will decrease as pH increases. The UV and visible absorption maxima are at 259.8 and 203.8 nm, respectively, in the acidic form, and at 262.4 and 209.7 nm, respectively, in the basic form. No absorption maxima are observed at wavelengths greater than 300 nm, indicating that florasulam has a low potential for phototransformation. The physical and chemical properties of florasulam relevant to the environment are summarized in Appendix I, Table 9.

For the primary transformation product from most transformation processes, 5-hydroxy-XDE-570 [*N*-(2,6-difluorphenyl)-8-fluoro-5-hydroxy (1,2,4)triazolo(1,5*c*)pyrimidine-2-sulphonamide], the solubility in reagent water at pH 5, 7 and 9 is 0.633, >450 and >800 g/L, respectively. 5-hydroxy-XDE-570 is very soluble at these pH values. The vapour pressure is 2.7×10^{-6} Pa at 25°C and the K is 2.63×10^{-6} Pa m^3 mol^{-1}, indicating that 5-hydroxy-XDE-570 is relatively non-volatile under field conditions and from water or moist soil surfaces. The log K_{ow} values are 0.32, –1.85 and –2.32 for pH 5, 7 and 9, respectively, indicating that bioconcentration or bioaccumulation is unlikely. The pK_a values of 5-hydroxy-XDE-570 are 4.53 and 7.22, indicating that the cation will predominate at pH <4.53, the anionic form will predominate at pH >7.22 and adsorption will decrease as pH increases. The physical and chemical properties of 5-hydroxy-XDE-570 relevant to the environment are summarized in Appendix I, Table 10.

5.2 Abiotic transformation

Florasulam does not hydrolyse at pH 5 and 7, but hydrolyses slowly at pH 9 with a first-order half-life ($t_{½}$) of 100 days at 25°C and 226 days at 20°C. Two major hydrolysis transformation products are formed at pH 9: 5-hydroxy-XDE-570 and a product that might be formed by addition of water to the triazolopyrimidine ring of the parent compound. The $t_{½}$ for phototransformation of florasulam on soil was estimated to be 62 days. The major phototransformation products on soil were 5-hydroxy-XDE-570 and one tentatively identified as aminyltriazolopyrimidine-florasulam. The $t_{½}$ for phototransformation of florasulam in water was estimated as 223 days in May and 88 days in June. The major phototransformation product in water was triazolopyrimidine sulphonic acid-florasulam. No significant amounts of volatile transformation products or CO_2 are produced by these transformation processes. Therefore, abiotic transformation is not an important route of transformation of florasulam.

5.3 Biotransformation

In aerobic soil, florasulam transforms by microbiological processes to produce a number of transformation products, non-extractable soil residues or CO_2. The half-life of florasulam ranges from 0.7 to 8.3 days. The major transformation products are 5-hydroxy-XDE-570, DFP-ASTCA, ASTCA and TSA. The half-life of 5-hydroxy-XDE-570 in aerobic soil ranges from 10 to 56 days. Florasulam is classified as non-persistent in aerobic soil, whereas the major transformation product, 5-hydroxy-XDE-570, is non-persistent to moderately persistent. Biotransformation is an important route of transformation of florasulam in the aerobic soil.

In aerobic water and sediment, the half-life of florasulam is three days. The major transformation products are 5-hydroxy-XDE-570, DFP-ASTCA and one tentatively identified as STCA. The half-life of 5-hydroxy-XDE-570 is 169 days. The bound residues reached 11% of applied and only 0.1–2.7% of the recovered radioactivity was present as $^{14}CO_2$ at the end of the study. Florasulam biotransforms to 5-hydroxy-XDE-570, which then transforms to DFP-ASTCA and the remaining transformation products. Florasulam is non-persistent and it is not expected to accumulate in natural sediments. 5-hydroxy-XDE-570 is persistent in the aerobic water and sediment system. Biotransformation is an important route of transformation of florasulam in aerobic aquatic systems.

In aerobic water and anaerobic sediment, the half-life of florasulam is 8.7–18 days. Florasulam is non-persistent to slightly persistent. The major transformation products are 5-hydroxy-XDE-570, DFP-ASTCA and a relatively unstable intermediate transformation product between the 5-hydroxy-XDE-570 and DFP-ASTCA, which is readily broken down to DFP-ASTCA. The half-lives of 5-hydroxy-XDE-570 were 69 to 244 days and, therefore, it is moderately persistent to persistent. The bound residues reached 9–11% of applied at study termination. Released $^{14}CO_2$ amounted to 1.9–8% of applied and there were no volatile organics. Florasulam biotranforms to 5-hydroxy-XDE-570, then subsequently to each of the other products. Biotransformation is an important route of transformation of florasulam in the aerobic water and anaerobic sediment system.

In anaerobic water and soil or water and sediment, the half-life of florasulam is <2 to 13 days. Florasulam is non-persistent. The major transformation product is 5-hydroxy-XDE-570, which is persistent. Florasulam biotransforms to 5-hydroxy-XDE-570, which further slowly transforms to the minor transformation product. No significant amounts of volatile transformation products are produced and the mineralization to CO_2 is minimal. Bound residue increases steadily, but very slowly, and never reaches 10% of the applied over the 12-month study period. Biotransformation is an important route of transformation in anaerobic aquatic environment.

In conclusion, florasulam is non-persistent in soil and water and sediment systems. The primary transformation product, 5-hydroxy-XDE-570, is non-persistent to moderately persistent in aerobic soil and persistent in aquatic systems. Biotransformation is an important route of transformation of florasulam.

5.4 Mobility

The results from the laboratory adsorption and desorption studies indicate that florasulam and the transformation product, 5-hydroxy-XDE-570, are highly to very highly mobile in soil. The soil column leaching studies show that florasulam and 5-hydroxy-XDE-570 have very high leaching potential.

The vapour pressure and K of florasulam and 5-hydroxy-XDE-570 indicate that they are relatively non-volatile under field conditions and non-volatile from a water surface or moist soil. This is confirmed by the results from the transformation studies that show that, under laboratory conditions, no volatile transformation products other than CO_2 are produced following application of florasulam to soil or aquatic systems.

The high solubility of florasulam in water indicates that it will primarily partition to the water phase. In addition, the relatively rapid biotransformation of florasulam in both soil and water and the low K_d and K_{oc} values indicate a low potential for accumulation of this compound in sediment. This was confirmed by the results of the aquatic biotransformation studies conducted with water and sediment systems.

The solubility of 5-hydroxy-XDE-570 is also high, which indicates that it will mainly remain in water phase and partitioning to sediment will be low. The adsorption coefficients, K_d and K_{oc}, indicate low adsorption of this compound to soil or sediment. This transformation product is persistent in both water and sediment.

5.5 Dissipation and accumulation under field conditions

Under field conditions, florasulam had DT_{50} values of 2–10 days and DT_{90} values of 16–34 days. No florasulam was detected after 2 months and, therefore, carry-over of the parent compound into the following season would not be expected. Florasulam is non-persistent. The major transformation product, 5-hydroxy-XDE-570, amounted for up to 59% of the amount applied under field conditions. 5-hydroxy-XDE-570 can persist and carry over. Florasulam and 5-hydroxy-XDE-570 have the potential to leach under conditions of excessive rainfall or irrigation.

5.6 Bioaccumulation

The log K_{ow} values were 1.00, –1.22 and –2.06 at pH 4, 7 and 10, respectively, for florasulam, and 0.32, –1.85 and –2.32 for pH 5, 7 and 9, respectively, for 5-hydroxy-XDE-570. These values indicate a negligible potential for bioaccumulation for both the parent compound and the major transformation product. Mammalian toxicology studies confirmed the low potential for the parent to accumulate.

5.7 Summary of fate and behaviour in the terrestrial environment

Florasulam does not hydrolyse at acidic or neutral pH, but hydrolyses slowly at basic pH. Phototransformation on soil occurs slowly. No significant amounts of volatile transformation products or CO_2 are produced by these transformation processes. In aerobic soil, florasulam is non-persistent. The primary transformation product, 5-hydroxy-XDE-570, is non-persistent to moderately persistent. Florasulam transforms by microbiological processes to produce a number of transformation products. Each of these transformation products, in turn, is transformed to either non-extractable soil residues or CO_2. Biotransformation is an important route of transformation of florasulam in the aerobic soil.

The results from the laboratory adsorption and desorption studies indicate that florasulam and 5-hydroxy-XDE-570 are highly to very highly mobile. Soil column leaching studies show that florasulam and 5-hydroxy-XDE-570 have very high leaching potential. Based on the vapour pressure and K, both the parent compound and the major transformation product are non-volatile.

Under field conditions, florasulam is non-persistent. Carry-over of this compound into the following season is not expected. The major transformation product, 5-hydroxy-XDE-570, can persist and carry over at high concentrations. Florasulam and 5-hydroxy-XDE-570 can leach when there is excessive rainfall or irrigation.

Based on log K_{ow} values, the potential for bioaccumulation for both the parent compound and the major transformation product is negligible.

The fate and behaviour data are summarized in Appendix I, Table 11, and the transformation products are summarized in Appendix I, Table 12.

5.8 Summary of fate and behaviour in the aquatic environment

Florasulam may enter aquatic environments through drift, run-off or leaching. Under field conditions, leaching to ground water can occur if there is excessive rainfall or irrigation.

Phototransformation of florasulam in water is slow. Abiotic transformations (i.e., hydrolysis and phototransformation) are not an important route of transformation of florasulam in aquatic environments.

Biotransformation is an important route of transformation of florasulam in aquatic environments. In water and sediment systems, florasulam is non-persistent and it is not expected to accumulate in natural sediments. 5-hydroxy-XDE-570 is persistent. Both the parent compound and the transformation product associate mainly with the water phase. Florasulam biotranforms to 5-hydroxy-XDE-570, which then transforms to each of the remaining transformation products. No significant amount of volatile transformation products and CO_2 are produced.

The fate and behaviour data are summarized in Appendix I, Table 13, and the transformation products are summarized in Appendix I, Table 14.

5.9 Expected environmental concentrations

5.9.1 Soil

The concentration of florasulam in a 15 cm depth of soil immediately after application to the soil surface at the maximum label rate of 5 g a.i./ha will be 0.0022 mg a.i./kg soil, assuming soil bulk density of 1.5 g/cm^3.

5.9.2 Aquatic systems

The concentration of florasulam in a 30 cm depth of water immediately after a direct overspray at the maximum label rate of 5 g a.i./ha will be 0.001667 mg a.i./L.

5.9.3 Vegetation and other food sources

Data that could be used to estimate the decrease in the concentration of florasulam on contaminated food sources for wildlife were not provided. Therefore, a scenario that assumes no transformation will occur on the surface of wildlife food sources was adopted. The estimated expected environmental concentrations (EECs) in vegetation were calculated using a nomogram from the United States Environmental Protection Agency (USEPA) (Appendix I, Table 8).Based on these values, the estimated EECs in the diet of non-target species immediately after an application of florasulam at 5 g a.i./ha, expressed as mg florasulam/kg dw diet, for representative non-target species are as follows:

- 0.6 (bobwhite quail);
- 0.17 (mallard ducks);
- 2.52 (rats);
- 2.51 (mice); and
- 3.31 (rabbits).

5.9.4 Monitoring data

Not applicable.

6.0 Effects on non-target species

Most of the studies with non-target organisms were conducted with florasulam technical. The end-use formulation, EF-1343, was the test material in the vascular plant seedling emergence and vegetative vigour studies, a daphnid acute study, a rainbow trout acute study, a green algae biomass study as well as four qualitative predatory and parasitic arthropod studies. The toxicity of 5-hydroxy-XDE-570 was examined in an earthworm acute study, a daphnid acute study, a rainbow trout acute study and a green algae acute study. The toxicity of the transformation products DFP-ASTCA, ASTCA, TSA, STA and STCA were also studied in an acute earthworm study.

6.1 Effects on terrestrial organisms

Florasulam is relatively non-toxic to bees on acute oral and contact basis. It is slightly toxic to Japanese quail on acute oral basis and practically non-toxic to Japanese quail and mallard duck on a dietary basis. Acute oral data indicate that florasulam is practically non-toxic to the rat and mouse, and that it has low toxicity to the rat and rabbit as demonstrated by acute inhalation data. Florasulam at rates up to 1300 mg a.i./kg soil (equivalent to 2790 kg a.i./ha) is not toxic to the earthworm on a 14-d acute basis. In the terrestrial vascular plant seedling emergence test, florasulam is toxic to the radish with a effective concentration against 25% of test organisms (EC_{25}) of 4.3 g a.i./ha, when applied as the formulation EF-1343. Significant phytotoxicity was observed on the dicot species with a most sensitive EC_{25} of 0.02 g a.i./ha on tomato. 5-hydroxy-XDE-570 is also relatively non-toxic to earthworm. The effects on terrestrial organisms are summarized in Appendix I, Table 15.

6.2 Effects on aquatic organisms

Florasulam is practically non-toxic to daphnids, rainbow trout and bluegill sunfish. The acute values for grass shrimp, oyster shell deposition and silverside indicated that florasulam is also practically non-toxic to crustaceans, mollusks and marine fish. It is, however, toxic to freshwater and marine algae as well as freshwater vascular plants. 5-hydroxy-XDE-570 is practically non-toxic to daphnids and rainbow trout, but it is toxic to green algae with a no observable effect concentration (NOEC) of 6.64 mg a.i./L. The effects on aquatic organisms are summarized in Appendix I, Table 16.

6.3 Effects on biological methods of sewage treatment

Not applicable.

6.4 Risk characterization

6.4.1 Environmental behaviour

Florasulam is non-persistent in soil and water. It is not expected to volatilize from water or moist soils. The principal route of transformation is biotransformation in both soil and water. Laboratory studies indicate that there is high to very high potential for florasulam to leach in soil and that leaching can be an important route of dissipation under field conditions when there is excessive seasonal rainfall or irrigation. Florasulam carry-over in the field is not expected. In water and sediment systems, florasulam is associated mainly with the water phase and is not expected to accumulate in natural sediments.

The major transformation product, 5-hydroxy-XDE-570, is non-persistent to moderately persistent in soil and persistent in aquatic systems. It is non-volatile. Laboratory studies indicate that it is also highly mobile and leachable in soil. In water and sediment systems, 5-hydroxy-XDE-570 is associated mainly with the water phase. It can persist and carry over in the field. Leaching to ground water can occur under field conditions when there is excessive rainfall or irrigation.

6.4.2 Terrestrial organisms

Margins of safety (MOSs) were calculated using the EEC values and the NOEC or an estimated NOEC equivalent to 1/10 of the median effective concentration (EC_{50}) or lethal concentration 50% (LC_{50}) for the most sensitive species per group.

Terrestrial invertebrates

The major route of exposure for earthworms is through ingested soil in treated fields. The MOS, based on a 14-d NOEC of 1300 mg a.i./kg soil, was calculated as 5.9×10^5. Thus, earthworms are not expected to be at risk from the proposed use of florasulam.

The major route of exposure to honeybees is through contact with contaminated plants. Using assumptions of Atkins et al. (1981), a NOEC of 100 µg a.i./bee is equivalent to a NOEC of 112 kg a.i./ha. Assuming a worst case of overspray, the EEC is the application rate, i.e., 5 g a.i./ha. The MOS is, therefore, 2.2×10^4, indicating that bees are not at risk from the proposed application of florasulam.

Avian species

The major route of exposure to birds is through ingestion of food contaminated by florasulam. The number of days of intake of florasulam required to reach the no observable effect dose level (NOEL) is 1188 days. The Japanese quail, therefore, is not at risk on an acute oral basis. The MOSs for dietary and reproductive effects, based on an 8-d NOEC of 5000 mg a.i./kg diet for Japanese quail and a reproductive NOEC of 1500 mg a.i./kg diet for bobwhite quail, are 8.3×10^3 and 2.5×10^3, respectively. Therefore, birds are not considered to be at risk from the proposed use of florasulam.

Small wild mammals

The major risk to small mammals is through ingestion of food sources contaminated by exposure to florasulam during and shortly after application. For acute oral toxicity (mouse), the MOS is expressed as 9.2×10^3 days of intake required to produce the equivalent of the dose administered to reach NOAEL in laboratory population. The MOS for dietary toxicity (rat) is 643 based on the NOAEL of 100 mg a.i./kg bw/d (1621 mg a.i./kg dw diet). Based on a NOAEL of 100 mg a.i./kg bw/d (parental and offspring), the MOS for reproductive toxicity (rat) is also 643. Therefore, wild mammals are not at risk from the proposed use of florasulam.

Terrestrial plants

The most sensitive plant species tested was the tomato. Based on the EC_{25} value of 0.02 g a.i./ha (plant vigour), the MOS is 0.004. Therefore, florasulam poses a very high risk to non-target terrestrial plants.

In conclusion, the proposed use of florasulam would not expect to pose risk to terrestrial invertebrates, wild birds and mammals. However, it will pose a very high risk to certain non-target plants (Appendix I, Table 17).

6.4.3 Aquatic organisms

Freshwater invertebrates and fish
Based on the overspray scenario and a 48-h NOEC of 174 mg a.i./L for daphnids and a 96-h NOEC of 100 mg a.i./L for rainbow trout, the MOSs for daphnids and rainbow trout are 1.04×10^5 and 6.00×10^5, respectively. Therefore, freshwater invertebrates and fish are not at risk from the proposed use of florasulam.

Freshwater plants
Similarly, based on the 72-h NOEC of 1.75 µg a.i./L for green algae biomass and a 14-d NOEC of 0.62 µg a.i./L for duckweed frond number, the MOSs for algae and duckweed are 1.05 and 0.37, respectively. Therefore, the use of florasulam poses a low risk to freshwater algae and a moderate risk to aquatic vascular plants.

Marine species
Among crustaceans, mollusks, marine fish and marine algae, the marine algae is the most sensitive group. Based on a 5-d NOEC of 22.8 mg a.i./L for marine diatom, the MOS is 1.37×10^4. Therefore, marine species are not at risk from the proposed use of florasulam.

In conclusion, the proposed use of florasulam would not pose a risk to the freshwater invertebrates and fish or various marine species. However, it will pose a low risk to freshwater alga and a moderate risk to aquatic vascular plants (Appendix I, Table 18).

6.4.4 Incident reports and additional considerations

Not applicable.

6.5 Risk mitigation

Leaching
Laboratory studies indicated a potential for mobility of florasulam and its major transformation product 5-hydroxy-XDE-570 in soil. In three field studies conducted under normal conditions of precipitation and irrigation, florasulam and the major transformation product did not leach. These three sites received irrigation equivalent to 110% of normal rainfall (30-year monthly average) during the growing season. Florasulam did, however, leach to a depth of 46 cm and 5-hydroxy-XDE-570 leached to a depth of 61 cm and, possibly, deeper depths at another site that received irrigation equivalent to 110% of normal rainfall plus typical irrigation for the growing season. This indicated that leaching can occur when excessive irrigation is applied. To mitigate the risk from leaching, the following label statement is required:

> "This product has the potential to leach. Do not apply excessive irrigation during and after application."

Persistence and carry-over of 5-hydroxy-XDE-570

The laboratory fate studies on the major transformation product, 5-hydroxy-XDE-570, indicate that it can be moderately persistent in soil and persistent in water and sediment systems. In the field dissipation study, no residue of 5-hydroxy-XDE-570 was detected 5 months after application at two test sites, but 17–28% was detected 15 months after application at two other test sites. This transformation product, therefore, has potential to persist and carry over. After three successive years of application, approximately 43% will persist in the soil. To mitigate the risk of persistence and carry-over of this transformation product, the following label statement is required:

> "Do not use in areas that were treated with this product during the previous season."

Spray drift

Exposure to florasulam will pose a very high risk to non-target terrestrial plants and a moderate risk to aquatic vascular plants. These risks can be mitigated by the establishment of terrestrial and aquatic buffer zones. A buffer zone of 32 m is required to protect terrestrial non-target wildlife habitats for ground applications of florasulam products at rate of 5 g a.i./ha. This value is based on the EC_{25} for tomato. A buffer zone of 5 m is required for protection of aquatic habitats. The following label statement is required:

> "Overspray or drift to sensitive habitats should be avoided. A buffer zone of 30 metres is required between the downwind edge of the boom and the closest edge of sensitive terrestrial habitats including forested areas, shelter belts, woodlots, hedgerows and shrub lands. A buffer zone of 5 metres is required between the downwind edge of the boom and the closest edge of sensitive aquatic habitats including sloughs, ponds, prairie potholes, lakes, rivers, streams, wetlands and wildlife habitats at the edge of these bodies of water. Do not contaminate these habitats when cleaning and rinsing spray equipment or containers.
>
> Do not apply during periods of dead calm or when winds are gusty.
>
> When a tank-mix is used, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank-mix."

7.0 Efficacy

7.1 Effectiveness

7.1.1 Intended uses

EF-1343 Suspension Concentrate Herbicide is proposed for use on spring wheat, including durum, spring barley and oats (in tank-mix only) at a rate of 100 mL/ha of product (5 g a.i./ha). The product is proposed for use in the prairie provinces and the Peace River region of British Columbia. Applied alone, EF-1343 is to be mixed with Agral 90 at 0.2% v/v. The following weeds are listed for control by EF-1343 applied alone:

- volunteer canola (*Brassica napus*) (including Roundup Ready and Liberty Link);
- common chickweed (*Stellaria media*);
- cleavers (*Galium aparine*);
- shepherd's purse (*Capsella bursa pastoris*);
- smartweed (*Polygonum persicaria*);
- stinkweed (*Thlaspi arvense*);
- wild buckwheat (*Polygonum convolvulus*); and
- wild mustard (*Sinapis arvensis*).

The following weeds are listed for suppression:

- hempnettle (*Galeopsis tetrahit*);
- redroot pigweed (*Amaranthus retroflexus*);
- annual sowthistle (*Sonchus oleraceus*); and
- perennial sowthistle (*Sonchus arvensis*).

EF-1343 is proposed for a single application per season, applied by ground equipment only, in a water volume of 50–100 L/ha on cereals from the 2-leaf stage up to and including the flag leaf extended stage. Weeds should be in the 2- to 4-leaf stage at the time of application.

Tank-mixes proposed for use with EF-1343 Suspension Concentrate Herbicide are summarized in Appendix I, Table 19, along with proposed adjuvants for use in the tank-mixes (Appendix I, Table 20).

7.1.2 Mode of action

Florasulam is a Group 2 herbicide that acts as an inhibitor of acetolactate synthase (ALS). ALS is found in the chloroplast where it catalyses branch chained amino acid biosynthesis. Plant growth is inhibited within 2 h following treatment with florasulam. While cell division and plant growth are quickly affected, ultimate death of the plant is slow. The exact relationship between branch chained amino acid biosynthesis and plant death is unknown.

7.1.3 Crops

EF-1343 is proposed for use on spring wheat, including durum, spring barley and oats *(in tank-mix only).*

7.1.4 Effectiveness against pests

7.1.4.1 EF-1343 at 5 g a.i./ha with Agral 90 at 0.2% v/v

Volunteer canola
A total of 27 trials conducted over three years summarized control of this species. Late season control averaged 83% control, for all varieties of canola pooled. Late season control of glufosinate tolerant and glyphosate tolerant canola varieties averaged 94%. The label claim for control of volunteer canola including Liberty Link and Roundup Ready herbicide tolerant varieties is acceptable.

Common chickweed
Control of common chickweed was reported in 16 trials conducted over three years. Late season control averaged 94% with the treatment of EF-1343 at 5 g a.i./ha with Agral 90 at 0.2%. The label claim for control of common chickweed is acceptable.

Cleavers
Control of cleavers was reported in 21 trials conducted over three years. Late season control averaged 96% with the treatment of EF-1343 at 5 g a.i./ha with Agral 90 at 0.2%. The label claim for control of cleavers is acceptable.

Smartweed
Control of smartweed was reported in 22 trials conducted over three years. Late season control averaged 96% with the treatment of EF-1343 at 5 g a.i./ha with Agral 90 at 0.2%. The label claim for control of smartweed is acceptable.

Stinkweed
Control of stinkweed was reported in 18 trials conducted over three years. Late season control averaged 92% with the treatment of EF-1343 at 5 g a.i./ha with Agral 90 at 0.2%. The label claim for control of stinkweed is acceptable.

Wild buckwheat
Control of wild buckwheat was reported in 20 trials conducted over three years. Late season control averaged 89% with the treatment of EF-1343 at 5 g a.i./ha with Agral 90 at 0.2%. The label claim for control of wild buckwheat is acceptable.

Wild mustard
Wild mustard control was reported in 11 trials conducted over two years. Late season control averaged 97% with the treatment of EF-1343 at 5 g a.i./ha with Agral 90 at 0.2%. The label claim for control of wild mustard is acceptable.

Shepherd's purse
Shepherd's purse control was reported in nine trials conducted over three years. Late season control averaged 95% with the treatment of EF-1343 at 5 g a.i./ha with Agral 90 at 0.2%. The label claim for control of shepherd's purse is acceptable.

Hempnettle
Control of hempnettle was reported in 13 trials conducted over three years. Late season control averaged 73% with the treatment of EF-1343 at 5 g a.i./ha with Agral 90 at 0.2%. The label claim for suppression of hempnettle is acceptable.

Redroot pigweed
Redroot pigweed control was reported in 12 trials conducted over two years. Late season control averaged 81% with the treatment of EF-1343 at 5 g a.i./ha with Agral 90 at 0.2%. The label claim for suppression of redroot pigweed is acceptable.

Annual sowthistle
Annual sowthistle control was reported in six trials conducted over two years. Late season control averaged 84% (based on 7 observations) with the treatment of EF-1343 at 5 g a.i./ha with Agral 90 at 0.2%. The label claim for suppression of annual sowthistle is acceptable.

Perennial sowthistle
Perennial sowthistle control was reported in 15 trials conducted over two years. The treatments were made to perennial sowthistle at leaf stages between 2- and 12-leaf. Late season control averaged 70% with the treatment of EF-1343 at 5 g a.i./ha with Agral 90 at 0.2%. The label claim for suppression of perennial sowthistle is acceptable with the addition of a label statement indicating that applications made at advanced leaf stages will reduce product effectiveness.

7.1.4.2 EF-1343 at 5 g a.i./ha + MCPA ester at 420 g a.i./ha

In addition to the data review described below, an additional review of a single year (1999) of bridging data was conducted to determine equivalency of a preformulated mixture of EF-1343 and MCPA ester with the proposed tank-mix to allow for consideration of data submitted by the applicant in support of the proposed tank-mix. The bridging data package consisted of a total of 29 field trials in which a direct comparison of the preformulated mixture and tank-mix was examined. The data demonstrated that the preformulated mixture and tank-mix perform similarly with respect to efficacy. Consequently, the efficacy data submitted with the formulated mixture was evaluated in support of the application to register the tank-mix.

Volunteer canola
Seven trials conducted in 1997 examined control of volunteer canola with a treatment of the formulated mixture of EF-1343 and MCPA ester. Late season control averaged 100% control for volunteer canola, all varieties pooled. The label claim for control of volunteer

canola with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

Control of glufosinate tolerant canola was examined in three trials conducted in 1998. Late season ratings averaged 99% control. The label claim for control of volunteer canola including Liberty Link canola with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

A total of 4 trials examined control of glyphosate tolerant canola with the formulated mixture of EF-1343 and MCPA ester. Late season ratings averaged 99% control for glyphosate tolerant canola. The label claim for control of Roundup Ready canola with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

Control of imazethapyr tolerant canola with the proposed tank-mix was recorded in eight trials. Late season ratings averaged 98% control for imazethapyr tolerant canola. The label claim for control of Smart canola with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

Common chickweed

Control of common chickweed was recorded in 13 trials conducted over two years. Late season control of common chickweed averaged 97% control. The label claim for control of common chickweed with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

Cleavers

Cleavers control was examined in a total of 18 trials conducted over two years. Late season control of cleavers averaged 98% control. The label claim for control of cleavers with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

Dandelion

Control of dandelion was recorded in a total of 14 trials conducted over two years. Late season control of seedling dandelion averaged 80% control with over half of the observations (8 out of a total of 13) providing control ratings between 60–80%. These results suggest that a claim of suppression of dandelion seedlings is more suitable than a claim of control. Late season control of dandelion rosettes averaged 65% control. The label claim for suppression of overwintered dandelion rosettes (less than 15 cm) with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

Flixweed

No data were summarized/submitted in support the request to label flixweed under the tank-mix instructions. In addition, this weed species does not appear on the list of weeds controlled by an application of EF-1343 alone, or the MCPA ester alone. Consequently, flixweed is not acceptable for labelling as controlled by the proposed tank-mix.

Hempnettle
Hempnettle control was summarized in a total of nine trials conducted over two years. Late season ratings for control of hempnettle averaged 85% control. The label claim for control of hempnettle with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

Lamb's quarters
A total of five trials conducted over two years examined control of lamb's quarters with the formulated mixture of EF-1343 and MCPA ester. Late season control of lamb's quarters averaged 99% control (based on 11 observations). The label claim for control of lamb's quarters with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

Ball mustard
No data were summarized/submitted in support of the tank-mix request for ball mustard; however, this species is listed for control on the MCPA ester label at a rate of 350 g a.i./ha suggesting that control should also be maintained by the proposed tank-mix. The label claim for control of ball mustard with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

Wild mustard
A total of 11 trials conducted over two years summarized control of wild mustard with the formulated mixture of EF-1343 and MCPA ester. Late season control of wild mustard averaged 99% control. The label claim for control of wild mustard with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

Redroot pigweed
Redroot pigweed control was examined in 16 trials over two years. Late season control of redroot pigweed averaged 93% control. The label claim for control of redroot pigweed with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

Common ragweed
No data for common ragweed were summarized/submitted in support of this tank-mix request; however, common ragweed is listed for control on the MCPA ester label at a rate of 350 g a.i./ha suggesting that this species should also be controlled by the proposed tank-mix. Consequently, the label claim for control of common ragweed with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

Shepherd's purse
A total of nine trials conducted over two years summarized control of shepherd's purse with the formulated mixture of EF-1343 and MCPA ester. Late season control of shepherd's purse averaged 99% control. The label claim for control of shepherd's purse with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

Smartweed
Smartweed control was reported in 14 trials from two years. Late season control of smartweed averaged 97% control. The label claim for control of smartweed with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

Stinkweed
Stinkweed control with the proposed tank-mix was reported in 14 trials conducted over two years. Late season control of stinkweed averaged 98% control. The label claim for control of stinkweed with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

Stork's bill
Control of stork's bill was summarized from a total of 10 trials over two years. Late season control of stork's bill averaged 86% with approximately a quarter of the observations (6 out of 26) providing control ratings less than 80%. These results, due to the inconsistency of the control results, suggest that a claim for control is unacceptable; however, with ratings between 60% and 80%, the claim of suppressing stork's bill is acceptable.

Wild buckwheat
A total of 18 trials conducted over two years examined control of wild buckwheat with the formulated mixture of EF-1343 and MCPA ester. Late season control of wild buckwheat averaged 91% control. The label claim for control of wild buckwheat with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

Canada thistle
A claim of suppression of Canada thistle (top growth control) was supported by results from 19 trials conducted over two years. Late season control of Canada thistle averaged 70% control. The label claim for suppression of Canada thistle (top growth control) with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

Round-leaved mallow
Round-leaved mallow control was examined in two trials conducted in 1998, with two additional trials (also conducted in 1998) reporting control of mallow species with the proposed tank-mix. This weed does not appear on the florasulam label or the MCPA ester label for control by either product alone, and insufficient data were submitted on which to formulate a decision as to the level of control offered by the proposed tank-mix. Consequently, this weed species is not acceptable for labelling at this time.

Annual sowthistle
A total of six trials conducted over two years examined control of annual sowthistle with the formulated mixture of EF-1343 and MCPA ester. Late season control of annual sowthistle averaged 87% control. The label claim for suppression of annual sowthistle with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

Perennial sowthistle
A total of 15 trials over two years examined control of perennial sowthistle with the formulated mixture of EF-1343 and MCPA ester. Late season control of perennial sowthistle averaged 79% control. The label claim for suppression of perennial sowthistle (top growth control) with the tank-mix of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha is acceptable.

7.1.4.3 EF-1343 at 5 g a.i./ha + Curtail M at 495 g a.i./ha

Canada thistle
Control of Canada thistle with the proposed tank-mix was reported in a total of 21 trials conducted over two years. Late season ratings averaged 86% control. The label claim for control of this species with the tank-mix of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha is acceptable.

Volunteer canola
Control of volunteer canola, including glufosinate tolerant, glyphosate tolerant, and imazethapyr tolerant varieties, was reported in a total of 17 trials conducted over two years. Late season ratings averaged 99% control. The label claim for control of volunteer canola including Roundup Ready, Liberty Link and Smart varieties with the tank-mix of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha is acceptable.

Common chickweed
Control of common chickweed was summarized in 13 trials conducted over two years. Late season ratings averaged 97% control. The label claim for control of this species with the tank-mix of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha is acceptable.

Cleavers
Control of cleavers was summarized in 18 trials over two years. Late season ratings averaged 98% control. The label claim for control of this species with the tank-mix of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha is acceptable.

Smartweed
Control of smartweed was summarized from 14 trials conducted over two years. Late season ratings averaged 98% control for smartweed. The label claim for control of this species with the tank-mix of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha is acceptable.

Stinkweed
Stinkweed control was examined in 14 trials over two years. Late season ratings averaged 99% control for stinkweed. The label claim for control of this species with the tank-mix of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha is acceptable.

Wild buckwheat

Wild buckwheat control was examined in 18 trials conducted over two years. Late season ratings averaged 96% control. The label claim for control of this species with the tank-mix of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha is acceptable.

Wild mustard

Wild mustard control was examined in 11 trials over two years. Late season ratings averaged 99% control. The label claim for control of this species with the tank-mix of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha is acceptable.

Hempnettle

Hempnettle control was reported in nine trials conducted over two years. Late season ratings averaged 88% control. The label claim for control of this species with the tank-mix of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha is acceptable.

Lamb's quarters

Lamb's quarters control was summarized for a total of seven trials over two years. Late season ratings averaged 96% control (based on eight observations). The label claim for control of this species with the tank-mix of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha is acceptable.

Shepherd's purse

Shepherd's purse control was reported in nine trials over two years. Late season ratings averaged 99% control. The label claim for control of this species with the tank-mix of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha is acceptable.

Redroot pigweed

Control of redroot pigweed was summarized for 14 trials conducted over two years. Late season ratings averaged 96% control (based on 16 observations) for redroot pigweed control. The label claim for control of this species with the tank-mix of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha is acceptable.

Annual sowthistle

Control of annual sowthistle was summarized for six trials over two years. Late season ratings averaged 97% control for annual sowthistle. The label claim for control of this species with the tank-mix of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha is acceptable.

Perennial sowthistle

Control of perennial sowthistle was summarized for 16 trials over two years. Late season ratings averaged 89% control for perennial sowthistle with four of the observations providing less than commercially acceptable control (i.e., <80% control). As a result, the label claim for this species with the tank-mix of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha is acceptable for suppression.

Dandelion

Control of dandelion was summarized from 18 trials conducted over two years. Late season ratings averaged 80% control for dandelion control, averaged over all stages of growth. The label claim for this species with the tank-mix of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha is modified to indicate suppression of dandelions (seedling and overwintered rosettes).

Stork's bill

Control of stork's bill was reported for 10 trials conducted over two years. Late season ratings averaged 90% control. The label claim for control of this species with the tank-mix of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha is acceptable.

Round-leaved mallow

Control of mallow species was summarized for six trials. Late season ratings averaged 85% control for a combination of results on *Malva pusilla* and *Malva neglecta*, with two of these observations indicating less than commercially acceptable control. The variability in results combined with the lack of species specific data does not support labelling of common mallow.

Ball mustard

No data were summarized/submitted in support of the request to label ball mustard for control by the proposed tank-mix. In addition, this weed does not appear on the list of weeds controlled by an application of EF-1343 alone, or Curtail M alone. Consequently, ball mustard is not acceptable for labelling as controlled by the proposed tank-mix.

Flixweed

No data for flixweed were summarized/submitted in support of this tank-mix request; however, flixweed is listed for control on the Curtail M label at the appropriate rate suggesting that this species should also be controlled by the proposed tank-mix. Consequently, the label claim for control of flixweed with the tank-mix of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha is acceptable.

7.1.4.4 EF-1343 + MCPA ester + Assert 300 SC

Wild oats

A total of 17 trials conducted over two years were summarized examining efficacy with the tank-mix of EF-1343 and MCPA ester + Assert 300 SC. Wild oat control with the tank-mix treatment of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha and Assert at 500 g a.i./ha (with Acidulate at 0.25% w/w) provided control of wild oats comparable to an application of Assert at 500 g a.i./ha (with Acidulate at 0.25% w/w) alone with late season control ratings of 97% and 92%, respectively. Broadleaf weed control was not affected by the tank-mix.

7.1.4.5 EF-1343 + MCPA ester + Horizon (56 g a.i./ha, 70 g a.i./ha)

A total of 28 trials conducted over three years were summarized examining efficacy with the tank-mix of EF-1343 and MCPA ester + Horizon at 56 and 70 g a.i./ha (with Score at 0.8 and 1.0% v/v, respectively).

Wild oats
A total of 18 trials conducted over two years summarized control of wild oats with the proposed tank-mix (Horizon at 56 g a.i./ha). Wild oat control with the tank-mix treatment of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha and Horizon at 56 g a.i./ha (Score at 0.8% v/v) provided control comparable to an application of Horizon at 56 g a.i./ha (Score at 0.8% v/v) alone with late season control ratings of 97% and 92%, respectively. Broadleaf weed control was not affected by the tank-mix.

Green foxtail
A total of 13 trials conducted over three years summarized control of green foxtail with the proposed tank-mix (Horizon at 72 g a.i./ha). Green foxtail control with the tank-mix treatment of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha and Horizon at 72 g a.i./ha (Score at 1.0% v/v) provided control comparable to an application of Horizon at 72 g a.i./ha (Score at 1.0% v/v) alone with late season ratings of 90% and 95%, respectively. Broadleaf weed control was not affected by the tank-mix.

7.1.4.6 EF-1343 + MCPA ester + Puma Super

Wild oats
A total of 20 trials conducted over two years summarized control of wild oats with the proposed tank-mix. Wild oat control with the tank-mix treatment of EF-1343 at 5 g a.i./ha with MCPA ester at 420 g a.i./ha and Puma Super at 92 g a.i./ha provided control comparable to an application of Puma Super at 92 g a.i./ha alone with late season control ratings of 94% and 97%, respectively. Broadleaf weed control was not affected by the tank-mix.

7.1.4.7 EF-1343 + Curtail M + Assert 300 SC

Wild oats
A total of 16 trials conducted over two years examined control of wild oats with the proposed tank-mix. Wild oat control with the tank-mix treatment of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha and Assert at 500 g a.i./ha (with Acidulate at 0.25% w/w) was comparable to an application of Assert at 500 g a.i./ha (with Acidulate at 0.25% w/w) alone with late season control ratings of 93% and 92%, respectively. Broadleaf weed control was not adversely affected by the tank-mix.

7.1.4.8 EF-1343 + Curtail M + Horizon (56 g a.i./ha, 70 g a.i./ha)

The applicant summarized a total of 20 trials conducted over two years. The majority of treatments were applied at the 1- to 4-leaf stage of wild oats, with a few trials at 2-tillers stage. Within the 20 trials conducted, 18 of the sites included Horizon at 56 g a.i./ha, and 11 of the sites included Horizon at 70 g a.i./ha.

Wild oats
Wild oat control with the tank-mix treatment of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha and Horizon at 56 g a.i./ha (Score at 0.8% v/v) was comparable to an application of Horizon at 56 g a.i./ha alone with late season control ratings of 95% and 98%, respectively. Broadleaf weed control was not adversely affected by the tank-mix.

Green foxtail
The applicant summarized a total of 15 trials conducted over three years. The majority of treatments were applied at the 2- to 5-leaf stage of green foxtail. Green foxtail control with the tank-mix treatment of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha and Horizon at 70 g a.i./ha (Score at 1.0% v/v) was comparable to an application of Horizon at 70 g a.i./ha alone with late season control ratings of 91 and 95%, respectively. Broadleaf weed control was not adversely affected by the tank-mix.

7.1.4.9 EF-1343 + Curtail M + Puma Super

Wild oats
The applicant summarized a total of 18 trials conducted over two years. The majority of treatments were applied at the 1- to 4-leaf stage of wild oats, with a few trials at the 2 tillers stage. Wild oat control with the tank-mix treatment of EF-1343 at 5 g a.i./ha with Curtail M at 495 g a.i./ha and Puma Super at 92 g a.i./ha provided control comparable to an application of Puma Super at 92 g a.i./ha alone with late season control ratings of 93 and 98%, respectively. Broadleaf weed control was not adversely affected by the tank-mix.

7.1.5 Total spray volume

The applicant applied for spray volume directions of 50 to 100 L/ha for EF-1343 applied alone, and in tank-mix with MCPA ester or Curtail M. Water volume for the three-way tank-mix combinations is 100 L/ha. The data submitted in support of the application to register EF-1343 applied alone did not examine spray volumes of 50 L/ha. Data in support of the tank-mixes with either MCPA ester or Curtail M did include treatments applied at 50 L/ha; however, the data were not summarized adequately to allow for a review of efficacy and crop tolerance of the 50 L/ha spray volume. As a result, the label directions must be modified to instruct a minimum spray volume of 100 L/ha.

7.2 Phytotoxicity to target plants (including different cultivars), or to target plant products

7.2.1 EF-1343 at 5 g a.i./ha + Agral 90 at 0.2% v/v

Crop tolerance for spring wheat, durum wheat and spring barley was assessed in both weed-free crop tolerance trials and efficacy trials. Crop phytotoxicity was assessed in the weed-free trials by recording visual tolerance parameters including: % chlorosis—visual, % injury—visual, % height—visual reduction, % delay maturity days—visual, visual injury, etc. A single quantitative measure of crop yield was taken at the end of the growing season. Both weed-free trials and efficacy trials were reported for all three crops and were conducted over two years.

Spring wheat
A total of 10 weed-free trials reported crop tolerance on spring wheat (including Canadian Prairie Spring [CPS] and Hard Red Spring [HRS]). All trials were conducted in 1997. Spring wheat varieties tested in the weed-free trials included: AC Taber, CDC Teal, Katepwa, AC Barrie and AC Karma. A total of 93 efficacy trials reported crop tolerance ratings on spring wheat. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values were comparable to the weed-free check treatment for both the 1× (5 g a.i./ha) and 2× (10 g a.i./ha) rates, 106% and 104%, respectively.

Spring barley
A total of 23 weed-free trials conducted over two years reported crop tolerance on spring barley (including 2-row, 6-row and hulless). Spring barley varieties tested in the weed-free trials included: Manley, Lacombe, Oxbow, Bedford, Harrington, B1602, Buck, Falcon, Condor, CDC Dawn and CDC Silky. A total of 23 efficacy trials reported crop tolerance ratings on spring barley. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values were comparable to the weed-free check treatment for both the 1× (5 g a.i./ha) and 2× (10 g a.i./ha) rates, 103% and 104%, respectively.

Durum wheat
A total of 23 weed-free trials (conducted over two years) reported crop tolerance on durum wheat. Durum wheat varieties tested in the weed-free trials included: Kyle, Sceptre and Plenty. A total of seven efficacy trials reported crop tolerance ratings on durum wheat. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values were comparable to the weed-free check treatment for both the 1× (5 g a.i./ha) and 2× (10 g a.i./ha) rates, 104% and 106%, respectively.

The data submitted support the application of EF-1343 at 5 g a.i./ha with Agral 90 at 0.5% v/v on spring wheat, durum wheat, and spring barley, in a minimum spray volume of 100 L/ha applied at the 2- to 6-leaf stage of the crop.

7.2.2 EF-1343 at 5 g a.i./ha + MCPA ester at 420 g a.i./ha

In addition to the data review described below, an additional review of a single year (1999) of bridging data was conducted to determine equivalency of a preformulated mixture of EF-1343 and MCPA ester with the proposed tank-mix to allow for consideration of data submitted by the applicant in support of the proposed tank-mix. The bridging data package consisted of 19 trials on spring wheat, 5 trials on durum wheat and 5 trials on spring barley. The data demonstrated that the preformulated mixture and tank-mix perform similarly with respect to crop tolerance. Consequently, the tolerance data submitted with the formulated mixture was evaluated in support of the application to register the tank-mix.

Crop tolerance for spring wheat, durum wheat, spring barley and oats was assessed in weed-free crop tolerance trials. Spring wheat and spring barley tolerance was also assessed in efficacy trials. Crop phytotoxicity was assessed in the weed-free trials by recording visual tolerance parameters including: chlorosis% visual, injury% visual, height% visual reduction, delay maturity days% visual, visual injury, etc. A single quantitative measure of crop yield was taken at the end of the growing season. Both weed-free trials and efficacy trials were conducted over two years.

Spring wheat
A total of 11 weed-free crop tolerance trials were summarized with a treatment of EF-1343 and MCPA ester at the proposed rate of 425 g a.i./ha. All trials were conducted in 1997. Both CPS and HRS varieties including AC Taber, AC Barrie, AC Karma, Teal and Katepwa were tested. In addition, 62 efficacy trials reported visual estimates of crop tolerance on spring wheat. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values were comparable to the weed-free check treatment for both the 1× (5 g a.i./ha florasulam + 420 g a.i./ha MCPA ester) and 2× (10 g a.i./ha florasulam + 840 g a.i./ha MCPA ester) rates, 106% and 105%, respectively.

Durum wheat
A total of 23 weed-free crop tolerance trials conducted over two years were summarized with a treatment of EF-1343 and MCPA ester at the proposed rate of 425 g a.i./ha. Varieties included Sceptre, Kyle and Plenty. Little to no visual injury was observed in the weed-free crop tolerance trials. Yield values were comparable to the weed-free check treatment for both the 1× and 2× rates, 105% and 103%, respectively.

Spring barley

A total of 25 weed-free crop tolerance trials conducted over two years were summarized with a treatment of EF-1343 and MCPA ester at the proposed rate of 425 g a.i./ha. Barley varieties tested included 2-row, 6-row and hulless, specifically, AC Lacombe, Manley, Buck, Oxbow, Harrington, B-1602, CDC Silky, Bedford, Falcon and CDC Dawn. In addition, 21 efficacy trials reported visual estimates of crop tolerance on spring barley. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values were comparable to the weed-free check treatment for both the 1× and 2× rates, 102% and 99%, respectively.

Oats

A total of 23 weed-free crop tolerance trials conducted over two years were summarized with a treatment of EF-1343 and MCPA ester at the proposed rate of 425 g a.i./ha. Varieties tested include: Boyer, Robert, Calibre and Riel. Little to no visual injury was observed in the weed-free crop tolerance trials. Yield values were comparable to the weed-free check treatment for both the 1× and 2× rates (96% each).

The data submitted for the tank-mix of EF-1343 at 5 g a.i./ha tank mixed with MCPA ester at 420 g a.i./ha suggest that adequate crop tolerance is observed when application is made to spring wheat, durum wheat, spring barley and oats in a minimum spray volume of 100 L/ha applied at the 2- to 6-leaf stage of the crop.

7.2.3 EF-1343 at 5 g a.i./ha + Curtail M at 495 g a.i./ha

Spring wheat

A total of 11 weed-free crop tolerance trials were summarized with a treatment of EF-1343 + Curtail M at the proposed rate of 5 g a.i./ha + 495 g a.i./ha. All trials were conducted in a single year (1997). All trials also reported crop tolerance at 2× rate. Spring wheat varieties included in the trials are: AC Taber, Teal, Katepwa, AC Barrie and AC Karma. In addition, 45 efficacy trials were summarized. Spring wheat varieties included in the trials were the following: AC Taber, Teal, Katepwa, AC Barrie, AC Karma, Roblin, Oslo, Biggar, Majestic, Domain, Pioneer and Makwan. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values were comparable to the weed-free check treatment for both the 1× (5 g a.i./ha EF-1343 + 495 g a.i./ha Curtail M) and 2× (10 g a.i./ha EF-1343 + 990 g a.i./ha Curtail M) rates, 104% and 105%, respectively.

Durum wheat

A total of 23 weed-free crop tolerance trials conducted over two years were summarized with a treatment of EF-1343 + Curtail M at the proposed rate of 5 g a.i./ha + 495 g a.i./ha. All trials also reported crop tolerance at 2× rate. Durum wheat varieties included in the trials were Kyle and Sceptre. In addition, two efficacy trials were summarized. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values were comparable to the weed-free check treatment for both the 1× and 2× rates, 106% and 100%, respectively.

Spring barley
A total of 23 weed-free crop tolerance trials conducted over two years were summarized with a treatment of EF-1343 + Curtail M at the proposed rate of 5 g a.i./ha + 495 g a.i./ha. All trials also reported crop tolerance at 2× rate. Spring barley varieties included in the trials were the following: Falcon, Manley, AC Lacombe, Bedford, Condor, Buck, Harrington, B1602, CDC Silky, Oxbow and CDC Down. In addition, 16 efficacy trials were summarized. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values were comparable to the weed-free check treatment for both the 1× and 2× rates, 101% and 100%, respectively.

Oats
A total of 23 weed-free crop tolerance trials conducted over two years were summarized with a treatment of EF-1343 + Curtail M at the proposed rate of 5 g a.i./ha + 495 g a.i./ha. Oat varieties included in the trials were the following: Boyer, Calibre, Robert and Riel. Visual estimates of crop injury at the early rating (≤21 DAT) indicate that slight damage may occur (up to 10% visual estimate); however, this appeared to have been outgrown by the later rating time (>21 DAT). Yield values were comparable to the weed-free check treatment for both the 1× and 2× rates, 98% and 100%, respectively.

7.2.4 EF-1343 + MCPA ester + Assert 300 SC

Spring wheat
A total of seven weed-free crop tolerance trials were summarized with a treatment of EF-1343 + MCPA ester + Assert 300 SC at the proposed rate of 5 g a.i./ha + 420 g a.i./ha + 500 g a.i./ha. All trials were conducted in a single year (1997). Efficacy trials were summarized reporting crop tolerance ratings. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values averaged 123% of the weed-free check treatment.

Durum wheat
A total of eight weed-free crop tolerance trials conducted over two years were summarized with a treatment of EF-1343 + MCPA ester + Assert 300 SC at the proposed rate of 5 g a.i./ha + 420 g a.i./ha + 500 g a.i./ha. Efficacy trials were also summarized reporting crop tolerance ratings. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values averaged 120% of the weed-free check treatment.

Spring barley
A total of eight weed-free crop tolerance trials conducted over two years were summarized with a treatment of EF-1343 + MCPA ester + Assert 300 SC at the proposed rate of 5 g a.i./ha + 420 g a.i./ha + 500 g a.i./ha. Efficacy trials were also summarized reporting crop tolerance ratings. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values averaged 108% of the weed-free check treatment.

7.2.5 EF-1343 + MCPA ester + Horizon

Spring wheat
A total of five weed-free crop tolerance trials (1997 only) were summarized with a treatment of EF-1343 + MCPA ester + Horizon at the proposed rate of 5 g a.i./ha + 420 g a.i./ha + 70 g a.i./ha with Score at 1.0% v/v. Efficacy trials were also summarized reporting crop tolerance ratings. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values averaged 123% of the weed-free check treatment.

Durum wheat
A total of eight weed-free crop tolerance trials conducted over two years were summarized with a treatment of EF-1343 + MCPA ester + Horizon at the proposed rate of 5 g a.i./ha + 420 g a.i./ha + 70 g a.i./ha with Score at 1.0% v/v. Little to no visual injury was observed in the weed-free crop tolerance trials with yield values averaging 126% of the weed-free check treatment.

7.2.6 EF-1343 + MCPA ester + Puma Super

Spring wheat
A total of five weed-free crop tolerance trials (1997 only) were summarized with a treatment of EF-1343 + MCPA ester + Puma Super at the proposed rate of 5 g a.i./ha + 420 g a.i./ha + 92 g a.i./ha. Efficacy trials were also summarized reporting crop tolerance ratings. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values averaged 124% of the weed-free check treatment.

Durum wheat
A total of eight weed-free crop tolerance trials conducted over two years were summarized with a treatment of EF-1343 + MCPA ester + Puma Super at the proposed rate of 5 g a.i./ha + 420 g a.i./ha + 92 g a.i./ha. Little to no visual injury was observed in the weed-free crop tolerance trials with yield values averaging 126% of the weed-free check treatment.

Spring barley
A total of eight weed-free crop tolerance trials conducted over two years were summarized with a treatment of EF-1343 + MCPA ester + Puma Super at the proposed rate of 5 g a.i./ha + 420 g a.i./ha + 92 g a.i./ha. Efficacy trials were also summarized reporting crop tolerance ratings. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values averaged 108% of the weed-free check treatment.

The data submitted in support of the three tank-mixes (EF-1343 + MCPA ester + Assert 300 SC; EF-1343 + MCPA ester + Horizon; EF-1343 + MCPA ester + Puma Super) suggest that adequate crop tolerance is observed when application is made to spring wheat, durum wheat and spring barley in a minimum spray volume of 100 L/ha at the 2- to 6-leaf stage of the crop.

7.2.7 EF-1343 + Curtail M + Assert 300 SC

Spring wheat

A total of five weed-free crop tolerance trials (1997) were summarized with a treatment of EF-1343 + Curtail M + Assert 300 SC at the proposed rate of 5 g a.i./ha + 495 g a.i./ha + 500 g a.i./ha. In addition, 11 efficacy trials were summarized reporting crop tolerance ratings. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values averaged 121% of the weed-free check treatment.

Durum wheat

A total of eight weed-free crop tolerance trials conducted over two years were summarized with a treatment of EF-1343 + Curtail M + Assert 300 SC at the proposed rate of 5 g a.i./ha + 495 g a.i./ha + 500 g a.i./ha. In addition, two efficacy trials were summarized reporting crop tolerance ratings. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values averaged 123% of the weed-free check treatment.

Spring barley

A total of eight weed-free crop tolerance trials conducted over two years were summarized with a treatment of EF-1343 + Curtail M + Assert 300 SC at the proposed rate of 5 g a.i./ha + 495 g a.i./ha + 500 g a.i./ha. In addition, 4 efficacy trials were summarized reporting crop tolerance ratings. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values averaged 111% of the weed-free check treatment.

7.2.8 EF-1343 + Curtail M + Horizon

Spring wheat

A total of five weed-free crop tolerance trials (1997 only) were summarized with a treatment of EF-1343 + Curtail M + Horizon at the proposed rate of 5 g a.i./ha + 495 g a.i./ha + 70 g a.i./ha with Score at 1.0% v/v. In addition, 12 efficacy trials were summarized reporting crop tolerance ratings. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values averaged 124% of the weed-free check treatment.

Durum wheat

A total of 8 weed-free crop tolerance trials conducted over two years were summarized with a treatment of EF-1343 + Curtail M + Horizon at the proposed rate of 5 g a.i./ha + 495 g a.i./ha + 70 g a.i./ha with Score at 1.0% v/v. Little to no visual injury was observed in the weed-free crop tolerance trials with yield values averaging 121% of the weed-free check treatment.

7.2.9 EF-1343 + Curtail M + Puma Super

Spring wheat
A total of five weed-free crop tolerance trials (1997 only) were summarized with a treatment of EF-1343 + Curtail M + Puma Super at the proposed rate of 5 g a.i./ha + 495 g a.i./ha + 92 g a.i./ha. In addition, 14 efficacy trials were summarized reporting crop tolerance ratings. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values averaged 123% of the weed-free check treatment.

Durum wheat
A total of eight weed-free crop tolerance trials conducted over two years were summarized with a treatment of EF-1343 + Curtail M + Puma Super at the proposed rate of 5 g a.i./ha + 495 g a.i./ha + 92 g a.i./ha. Little to no visual injury was observed in the weed-free crop tolerance trials with yield values averaging 122% of the weed-free check treatment.

Spring barley
A total of eight weed-free crop tolerance trials conducted over two years were summarized with a treatment of EF-1343 + Curtail M + Puma Super at the proposed rate of 5 g a.i./ha + 495 g a.i./ha + 92 g a.i./ha. In addition, 4 efficacy trials were summarized reporting crop tolerance ratings. Little to no visual injury was observed in either the weed-free crop tolerance trials or the efficacy trials. Yield values averaged 109% of the weed-free check treatment.

The data submitted in support of the four tank-mixes (EF-1343 + Curtail M; EF-1343 + Curtail M + Assert 300 SC; EF-1343 + Curtail M + Horizon; EF-1343 + Curtail M + Puma Super) suggest that adequate crop tolerance is observed when application is made to spring wheat, durum wheat, spring barley or oats (Curtail tank-mix only) in a minimum spray volume of 100 L/ha at the 2- to 6-leaf stage of the crop.

7.3 Observations on undesirable or unintended side effects

7.3.1 Impact on succeeding crops

The proposed crop rotation instructions for EF-1343 Suspension Concentrate Herbicide allow for seeding the following year to barley, canola, forage grasses, oats, peas, rye or wheat, or fields can be summer fallowed. Six field trials were conducted in support of the proposed recrop instructions: two trials in 1996 and four trials in 1997. Trials were conducted in the provinces of Alberta (two trials), Saskatchewan (two trials) and Manitoba (two trials) and examined rates of 1× and 2×. Only canola and peas were examined in the field trials with scientific rationales and plantback data provided for wheat, barley and other monocot crops.

In the five trials examining recrop effects on canola, the crop was planted at 10–11 months following the application of EF-1343 alone or in tank-mix. Parameters measured included visual % injury, delay in maturity, growth inhibition, stand reduction and crop yield (reported in three trials). Yield was consistently above the untreated check.

Peas were planted at 10–11 months following an application of EF-1343 alone or in tank-mix, in a total of five trials with four trials reporting yield. In addition to yield, parameters assessed included visual % injury, delay in maturity, growth inhibition and stand reduction. Yield values were consistently equal to or greater than the untreated check treatment for EF-1343 at the 1× and 2× rates.

The rationale provided for inclusion of wheat and barley in the crop rotation studies is acceptable, along with the plantback data provided.

The information provided for oats, rye and forage grasses as rotational crops is not acceptable.

7.3.2 Impact on adjacent crops

The applicant has included the following label statements under the General Use Precautions section of the EF-1343 Suspension Concentrate Herbicide label:

> "Do not apply EF-1343 directly to, or otherwise permit it to come in direct contact with, susceptible crops or desirable plants including alfalfa, edible beans, canola, flowers and ornamental, lentils, lettuce, peas, potatoes, radishes, soybeans, sugar beets, sunflowers, tomatoes or tobacco."
>
> "Do not apply where proximity of susceptible crops (e.g., canola and legumes) or other desirable plants is likely to result in exposure to spray or spray drift."

The proposed label statements should adequately address concerns regarding impact on adjacent crops.

7.4 Economics

The applicant did not address this section in the data submission.

7.5 Sustainability

7.5.1 Survey of alternatives

See Appendix I, Table 21.

7.5.2 Contribution to risk reduction

The applicant did not address this section in the data submission.

7.5.3 Information on the occurrence or possible occurrence of the development of resistance

In the interest of resistance management, the EF-1343 Suspension Concentrate Herbicide label will be modified to include the following statements, as outlined in Regulatory Directive DIR99-06, *Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action*.

Resistance management recommendations
For resistance management, EF-1343 is a Group 2 herbicide. Any weed population may contain or develop plants that are naturally resistant to EF-1343 and other Group 2 herbicides. The resistant biotypes may dominate the weed population if these herbicides are used repeatedly in the same field. Other resistance mechanisms that are not linked to site of action, but specific for individual chemicals, such as enhanced metabolism, may also exist. Appropriate resistance management strategies should be followed.

To delay herbicide resistance:

- Where possible, rotate the use of EF-1343 or other Group 2 herbicides with different herbicide groups that control the same weeds in a field.
- Use tank-mixes with herbicides from a different group when such use is permitted.
- Base herbicide use on an integrated pest management program that includes scouting, historical information related to herbicide use and crop rotation, and considers tillage (or other mechanical), cultural, biological and other chemical control practices.
- Monitor treated weed populations for resistance development.
- Prevent movement of resistant weed seeds to other fields by cleaning harvesting and tillage equipment and planting clean seed.
- Contact your local extension specialist or certified crop advisors for any additional pesticide resistance management and integrated weed management recommendations for specific crops and weed biotypes.
- For further information or to report suspected resistance, contact Dow AgroSciences at 1 800 667-3852.

7.6 Conclusions

Adequate efficacy and crop tolerance data have been provided to support application of EF-1343 Suspension Concentrate Herbicide on spring wheat, including durum, and spring barley alone and in proposed tank-mixes. Efficacy and crop tolerance is acceptable for application of EF-1343 on oats in tank-mixes as appropriate. Data submitted support application once per season to cereals at the 2- to 6-leaf stage in a minimum water volume of 100 L/ha. Recropping data submitted for review support planting of barley, canola, peas or wheat the year following application of EF-1343 (or field can be summer fallowed). Data was not submitted to support a rainfast statement indicating that EF-1343 is rainfast 1 h after application; as a result, this statement is not acceptable.

Tank mixtures for which adequate efficacy and crop tolerance were demonstrated include the following:

- EF-1343 + MCPA ester;
- EF-1343 + Curtail M Herbicide;
- EF-1343 + MCPA ester + Assert 300 SC;
- EF-1343 + MCPA ester + Horizon Herbicide;
- EF-1343 + MCPA ester + Puma Super Herbicide;
- EF-1343 + Curtail M + Assert 300 SC;
- EF-1343 + Curtail M + Horizon Herbicide; and
- EF-1343 + Curtail M + Puma Super Herbicide.

8.0 Toxic Substances Management Policy considerations

During the review of florasulam, the PMRA has taken into account the federal Toxic Substances Management Policy and has followed the Regulatory Directive DIR99-03. It has been determined that this product does not meet TSMP Track 1 criteria.

- Florasulam does not meet the TSMP Track 1 criteria for persistence. The values for half-life in water and sediment (3–18 days) and soil (0.7–8.3 days) are below the TSMP Track 1 cut-off criteria for water (≥ 182 days), soil (≥ 182 days) and sediment (≥ 365 days). Because it is relatively non-volatile, a phototransformation study in air was not triggered.

- Florasulam is not bioaccumulative. Studies have shown that the *n*-octanol–water partition coefficient (log K_{ow}) is 1.00, –1.22 and –2.06 for pH 4, 7 and 10, respectively, which is below the TSMP Track 1 cut-off criterion of ≥ 5.0. A bioconcentration study in fish was not triggered.

- Mammalian toxicology studies indicated a low potential for accumulation. The toxicity of florasulam is described in sections 3.0 and 6.0 and Appendix I.

- 5-hydroxy-XDE-570 is the primary transformation product in laboratory fate studies and it is the only major transformation product in the field. This transformation product does not meet the TSMP Track 1 criteria because it does not bioaccumulate.
- All formulants in the three formulated products, EF-1343 Manufacturing Concentrate, EF-1343 Suspension Concentrate Herbicide and EF-1440 Manufacturing Concentrate, are either USEPA list 3 or 4, except for an antifoam compound, polydimethyl siloxane, which is not included in the lists. The concentration of this formulant ranges from 0.02 to 0.18% by weight. No known USEPA list 1 or 2 formulants are contained in these formulations.
- The formulated products do not contain any byproducts or microcontaminants that are known to be TSMP Track 1 substances. Impurities of toxicological concern are not expected to be present in the raw materials nor are they expected to be generated during the manufacturing process.

9.0 Regulatory decision with additional data requirements

Florasulam Technical, the manufacturing end-use products EF-1440 Manufacturing Concentrate and EF-1343 Manufacturing Concentrate, and the end-use product EF-1343 Suspension Concentrate Herbicide are proposed for full registration for use on spring wheat, including durum, spring barley and oats (in tank-mix only) with the following MRLs: wheat (0.01 ppm), barley (0.01 ppm) and oats (0.01 ppm), pursuant to Section 13 of the PCP Regulations.

List of abbreviations

ADI	acceptable daily intake
a.i.	active ingredient
ALAT	alanine aminotransferase
ALP	alkaline phosphatase
ALS	acetolactate synthase
AN-labelled	aniline-labelled
ARfD	acute reference dose
BBCH	BASF, Bayer, Ciba-Geigy and Hoechst
bw	body weight
bwg	body-weight gain
CAS	Chemical Abstracts Service
CD	caesarian derived
C_{max}	peak plasma concentration
$C_{½max}$	one-half maximum plasma concentration
CPS	Canadian Prairie Spring
CSFII	Continuing Survey of Food Intake by Individuals
d	day(s)
DAT	day(s) after treatment
DEEM-FCID™	Dietary Exposure Evaluation Model software with the Food Commodity Intake Database
DT_{50}	time required for non first-order 50% dissipation
DT_{90}	time required for non first-order 90% dissipation
dw	dry weight of diet
E. coli	*Escherichia coli*
EC_{25}	concentration effective against 25% of test organisms
EC_{50}	median effective concentration
EEC	expected environmental concentration
EP	end-use product
F_1	1st generation offspring
F_2	2nd generation offspring
fw	fresh weight
GAP	good agricultural practice
GC	gas chromatography
GC-MSD	gas chromatography mass selective detection
GIT	gastrointestinal tract
GSD	geometric standard deviation
K	Henry's law constant
HCT	hematocrit
HD	high dose
HDPE	high density polyethylene
HDT	highest dose tested
HGB	hemoglobin
HGPRT	hypoxanthine guanine phosphoribosyl transferase
HPLC	high performance liquid chromatography

HRS	Hard Red Spring
ILV	independent laboratory validation
K_d	Freundlich adsorption coefficient
K_{oc}	organic carbon adsorption coefficient
K_{ow}	*n*-octanol–water partition coefficient
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LD	low dose
LOAEL	lowest observed adverse effect level
LOD	limit of detection
LOQ	limit of quantitation
LSC	liquid scintillation counting
MIS	maximum irritation score
MAS	maximum average score (for 24, 48 and 72 h)
MOE	margin of exposure
MOS	margin of safety
MRL	maximum residue limit
MS	mass spectrometry
MSD	mass selection detection
MTBE	methyl tertiary butyl ether
NOAEL	no observed adverse effect level
NOEC	no observable effect concentration
NOEL	no observable effect dose level
NZW	New Zealand white
P_1	1st generation parental animals
P_2	2nd generation parental animals
PBI	plantback interval
PCP	pest control product
PET	polyethylene terephthalate
pH	$-\log_{10}$ hydrogen ion concentration
PH-labelled	phenyl-labelled
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
pK_a	acid dissociation constant
PPE	personal protective equipment
ppm	parts per million
RAC	raw agricultural commodity
RBC	red blood cells
RSD	relative standard deviation
SD	standard deviation
SG	specific gravity
$t_{1/2}$	first-order half-life
TGAI	technical grade active ingredient
TP-labelled	triazolopyrimidine-labelled
TLC	thin layer chromatography
TRR	total radioactive residue

TSMP	Toxic Substances Management Policy
μg	microgram
μL	microlitre
USEPA	United States Environmental Protection Agency
v/v	volume per volume

Appendix I Summary tables

Table 1 Methods for analysis of the active substance as manufactured

Product	Analyte	Method no.	Method type	Recovery (%)	RSD (%)	Method acceptability
Technical	Florasulam	EU-AM-97-001	HPLC–UV	99.4	0.3	Acceptable
Technical	Major impurities	EU-AM-97-002	HPLC–UV	97–102	0.7–7.6	Acceptable

Table 2 Method for formulation analysis

<table>
<tr><th>Product</th><th>Analyte</th><th>Method no.</th><th>Method</th><th>Mean recovery</th><th>SD</th><th>Method acceptability</th></tr>
<tr><td>EF-1440 Manufacturing Concentrate</td><td>Florasulam</td><td colspan="5">Not required for manufacturing concentrate</td></tr>
<tr><td>EF-1343 Manufacturing Concentrate and EF-1343 Suspension Concentrate</td><td>Florasulam</td><td>EU-AM-96-005</td><td>HPLC</td><td>98% (<i>n</i> = 7)</td><td>0.83% (<i>n</i> = 5)</td><td>Acceptable</td></tr>
</table>

Table 3 Methods for residue analysis

<table>
<tr><td colspan="7">MULTI-RESIDUE METHODS FOR RESIDUE ANALYSIS
Protocols from existing multi-residue methods were not found to be suitable for the determination of florasulam.</td></tr>
<tr><td colspan="7">METHODS FOR RESIDUE ANALYSIS OF PLANTS AND PLANT PRODUCTS
Data gathering method
Immunoassay method
Limit of quantitation (LOQ) = 0.01 ppm for grain and 0.05 ppm for forage, hay, straw, immature green plants and immature dry plants (wheat, barley and oat)
Residue of concern: The residue of concern (ROC) was defined as the parent florasulam.</td></tr>
<tr><th>Matrix</th><th>Wheat, grain</th><th>Wheat, forage</th><th>Wheat, hay</th><th>Wheat, straw</th><th>Wheat, immature green plants</th><th>Wheat, immature dried plants</th></tr>
<tr><td>Spiking levels (ppm)</td><td>0.01–0.2</td><td>0.05–1.0</td><td>0.05–1.0</td><td>0.05–1.0</td><td>0.05–1.0</td><td>0.05–1.0</td></tr>
<tr><td>Range of recoveries (%)</td><td>76–136
(<i>n</i> = 12)</td><td>90–120
(<i>n</i> = 12)</td><td>81–110
(<i>n</i> = 12)</td><td>88–114
(<i>n</i> = 12)</td><td>96–122
(<i>n</i> = 12)</td><td>108–126
(<i>n</i> = 12)</td></tr>
<tr><td>Recovery mean ± SD (%)</td><td>97 ± 13</td><td>105 ± 4</td><td>93 ± 6</td><td>98 ± 6</td><td>113 ± 7</td><td>116 ± 5</td></tr>
</table>

Appendix I Summary tables

Table 1 Methods for analysis of the active substance as manufactured

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Technical	Major impurities	EU-AM-97-002	HPLC-UV	97–102	0.7–7.6	Acceptable

Table 2 Method for formulation analysis

Product	Analyte	Method no.	Method	Mean recovery	SD	Method acceptability
EF-1440 Manufacturing Concentrate	Florasulam	Not required for manufacturing concentrate				
EF-1343 Manufacturing Concentrate and EF-1343 Suspension Concentrate	Florasulam	EU-AM-96-005	HPLC	98% (*n* = 7)	0.83% (*n* = 5)	Acceptable

Table 3 Methods for residue analysis

MULTI-RESIDUE METHODS FOR RESIDUE ANALYSIS
Protocols from existing multi-residue methods were not found to be suitable for the determination of florasulam.

METHODS FOR RESIDUE ANALYSIS OF PLANTS AND PLANT PRODUCTS
Data gathering method
Immunoassay method
Limit of quantitation (LOQ) = 0.01 ppm for grain and 0.05 ppm for forage, hay, straw, immature green plants and immature dry plants (wheat, barley and oat)
Residue of concern: The residue of concern (ROC) was defined as the parent florasulam.

Matrix	Wheat, grain	Wheat, forage	Wheat, hay	Wheat, straw	Wheat, immature green plants	Wheat, immature dried plants
Spiking levels (ppm)	0.01–0.2	0.05–1.0	0.05–1.0	0.05–1.0	0.05–1.0	0.05–1.0
Range of recoveries (%)	76–136 (*n* = 12)	90–120 (*n* = 12)	81–110 (*n* = 12)	88–114 (*n* = 12)	96–122 (*n* = 12)	108–126 (*n* = 12)
Recovery mean ± SD (%)	97 ± 13	105 ± 4	93 ± 6	98 ± 6	113 ± 7	116 ± 5

<table>
<tr><td colspan="7">Confirmatory method
Capillary gas chromatography with mass selective detection (GC–MSD)
LOQ = 0.01 ppm for grain and 0.05 ppm for forage, hay, straw, immature green plants and immature dry plants (wheat, barley and oat)
ROC: The ROC was defined as the parent florasulam.</td></tr>
<tr><th>Matrix</th><th>Wheat, grain</th><th>Wheat, forage</th><th>Wheat, hay</th><th>Wheat, straw</th><th>Immature green plants</th><th>Immature dried plants</th></tr>
<tr><td>Spiking levels (ppm)</td><td>0.01–0.1</td><td>0.05–0.50</td><td>0.05–0.50</td><td>0.05–0.25</td><td>0.05–0.50</td><td>0.05–0.25</td></tr>
<tr><td>Range of recoveries (%)</td><td>74–83
(<i>n</i> = 5)</td><td>74–80
(<i>n</i> = 4)</td><td>79–92
(<i>n</i> = 4)</td><td>85–92
(<i>n</i> = 4)</td><td>71–79
(<i>n</i> = 4)</td><td>81–96
(<i>n</i> = 4)</td></tr>
<tr><td>Recovery mean ± SD (%)</td><td>80 ± 4</td><td>74 ± 2</td><td>84 ± 6</td><td>88 ± 3</td><td>75 ± 4</td><td>89± 8</td></tr>
<tr><td colspan="7">Enforcement method
Enforcement method is equivalent to confirmatory method.
Independent laboratory validation (ILV)
ILV indicated good reliability and reproducibility.</td></tr>
</table>

Table 4 Methods for environmental residue analysis

Matrix	Method	Fortification level (µg/kg)	Overall mean recovery (%)				LOQ (µg/kg)	Method acceptability
			Parent (XDE-570)	RSD (%)	5-OH XDE-570	RSD (%)		
Soil	HPLC–MS	0.05–50	95 (*n* = 20)	6.7	80 (*n* = 20)	10.6	0.05	Acceptable
	GC–MSD	1–100	85 (*n* = 19)	10–11	86 (*n* = 19)	7–20	0.93, 0.61	Acceptable
Sediment	The applicant requested to use the soil method and provided scientifically sound rationale based on the chemical and physical properties and the extraction efficiencies using ^{14}C material in soil and in sediment.							Waiver accepted
Drinking water	HPLC–UV	0.05–1.00	99 (*n* = 20)	5.2	89 (*n* = 20)	10.3	0.05	Acceptable
Plant	The applicant requested that the analytical method used to quantify XDE-570 and metabolites in crops (wheat and barley) be extended to other flora.							Section 2.3.1
Animal matrix	The method was not requested, as the potential for bioaccumulation is low due to the very low log K_{ow} values (–2.32 to 1.00) for both parent and transformation product at pH 4–9.							

Table 5 Toxicology summary

NOTE: Hypertrophy of the epithelial cells of the collecting ducts was observed in all species tested. With the exception of elevated serum bicarbonate levels in the HD males in the two-year rat dietary study, there were no toxicologically relevant clinical chemistry findings (serum creatinine, nitrogen or electrolyte levels) to correlate with urinalysis findings in the rat or with hypertrophy of the epithelial cells in the mouse, rat and dog; or to indicate an impairment of renal function in any species tested. There was no significant increased incidence of cellular degeneration or necrosis evident in the kidneys in any species tested. Renal function did not appear to be compromised in any species tested and continued ingestion of the test substance did not result in significant deterioration of renal function nor in renal tumours. In mice, the severity of the hypertrophy increased from very slight following 90 d to slight following 12 and 24 months of exposure. In rats, it appeared to become more pronounced over time from 3 to 24 months. In dogs, the severity (slight) did not appear to increase with prolonged exposure.

RAT: METABOLISM: ^{14}C-XR-570 uniformly labelled in the aniline ring (both sexes) or labelled at the 9 position on the triazolo-pyrimidine ring (males only)

Absorption: Following single or repeat oral LD, or single oral HD administration, ^{14}C-XR-570 was extensively and rapidly absorbed in both sexes. Peak plasma concentrations (C_{max}) were achieved within 0.5–1 h following single LD and HD administration. Estimated proportion of administered dose absorbed was ~90–93% following single or repeat LD administration and ~82–86% following single HD administration. Bile absorption accounted for 1% of the administered dose by 24 h. Data suggest a saturation of absorption and saturable renal excretion at the HD and more rapid and efficient removal at the LD.

Distribution: Highest residues levels were observed in skin and carcass; however, mean recovery of radioactivity in tissues and carcass at sacrifice (at 168 h post-dosing) was less than 0.6% of administered dose for all dose groups indicating little potential for accumulation. The apparent volume of distribution was increased at the HD, which may suggest increased binding to tissues at this dose level.

Metabolism: Major component in urine and fecal extracts was identified as the unchanged parent compound, XR-570, representing ~77–85% of administered dose. Two other metabolites found in excreta were characterized as OH-phenyl-XR-570 (~3–10% of the administered dose) and a sulfate conjugate of OH-phenyl-XR-570 (~2–4% of the administered dose). Two minor peaks were not identified (neither represented greater than 0.32% of the administered dose). Sulfate conjugate of the OH-phenyl-XR-570 was not observed in fecal extracts and was either not detected or not quantifiable in urine of females at any dose level. Metabolites in urine and feces revealed no evidence of hydrolysis of sulphonamide bridge. XR-570 was metabolized only slightly in the kidneys, liver and blood with the parent compound accounting for greater than 90% of the recovered radioactivity in these tissues at C_{max} and $C_{½max}$. In the bile, the unchanged parent compound, XDE-570 accounted for 0.09% of the administered dose.

Excretion: Excretion was rapid, with a majority of radioactivity being eliminated within 12 h post-dosing via urine (>80 and 60% at the LD and HD, respectively) and within 24 h post-dosing via feces (3–6 and 11–15% at the LD and HD, respectively). Urinary excretion rate half-life ($t_{½}$) was ~3–4 and 5 h at the LD and HD, respectively. Major route of excretion was via urine, accounting for ~90–92 and 81–85% of administered dose at the LD and HD, respectively. Fecal excretion accounted for ~5–7 and 14–17% of administered dose at the LD and HD, respectively. By 24 h, less than 0.5% of administered dose was excreted via expired air and ~1% was excreted by the bile. No significant differences in absorption, distribution, metabolism or excretion, or changes in pharmacokinetic parameters between the LD aniline labelled and pyrimidine labelled groups. Absorption, distribution, metabolism and excretion not influenced by repeat LD oral administration. No significant sex-related difference in absorption, distribution, metabolism or excretion following single or repeat LD administration or single HD administration.

STUDY	SPECIES OR STRAIN AND DOSES	LD_{50}, LC_{50}, MIS OR MAS	TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS
ACUTE STUDIES: Technical florasulam (XDE-570)			
Oral	CD-1 mice 5 mice/sex/dose **Dose levels:** 600 (♀ only), 2000 (♀ only) or 5000 (both sexes) mg/kg bw	LD_{50} greater than 5000 mg/kg bw for both sexes	No mortalities at 600 or 2000 mg/kg bw. At 5000 mg/kg bw, 2 ♀ died at approximately 24 h. No treatment-related clinical observations, necropsy findings or changes in bw **LOW TOXICITY**

Confirmatory method
Capillary gas chromatography with mass selective detection (GC–MSD)
LOQ = 0.01 ppm for grain and 0.05 ppm for forage, hay, straw, immature green plants and immature dry plants (wheat, barley and oat)
ROC: The ROC was defined as the parent florasulam.

Matrix	Wheat, grain	Wheat, forage	Wheat, hay	Wheat, straw	Immature green plants	Immature dried plants
Spiking levels (ppm)	0.01–0.1	0.05–0.50	0.05–0.50	0.05–0.25	0.05–0.50	0.05–0.25
Range of recoveries (%)	74–83 (*n* = 5)	74–80 (*n* = 4)	79–92 (*n* = 4)	85–92 (*n* = 4)	71–79 (*n* = 4)	81–96 (*n* = 4)
Recovery mean ± SD (%)	80 ± 4	74 ± 2	84 ± 6	88 ± 3	75 ± 4	89± 8

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STUDY	SPECIES OR STRAIN AND DOSES	LD_{50}, LC_{50}, MIS OR MAS	TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS
ACUTE STUDIES: Technical florasulam (XDE-570)			
Oral	CD-1 mice 5 mice/sex/dose **Dose levels:** 600 (♀ only), 2000 (♀ only) or 5000 (both sexes) mg/kg bw	LD_{50} greater than 5000 mg/kg bw for both sexes	No mortalities at 600 or 2000 mg/kg bw. At 5000 mg/kg bw, 2 ♀ died at approximately 24 h. No treatment-related clinical observations, necropsy findings or changes in bw **LOW TOXICITY**

STUDY	SPECIES OR STRAIN AND DOSES	LD$_{50}$, LC$_{50}$, MIS OR MAS	TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS
Oral	Fischer 344 rats 5 rats/sex/dose **Dose levels:** 1000, 3000 or 6000 mg/kg bw	LD$_{50}$ greater than 6000 mg/kg bw for both sexes	No mortalities at 1000 or 3000 mg/kg bw. At 6000 mg/kg bw, 1 male (d 7) and 2 ♀ (d 2 and d 7) died (bw loss prior to death). No treatment-related clinical observations, necropsy findings or changes in bw **LOW TOXICITY**
Dermal: Limit test	New Zealand white (NZW) rabbits 5 rabbits/sex **Dose level:** 2000 mg/kg bw	LD$_{50}$ greater than 2000 mg/kg bw for both sexes	No mortalities and no treatment-related clinical observations, necropsy findings or changes in bw **LOW TOXICITY**
Inhalation: Limit test (4-h nose-only)	Fischer 344 rats 5 rats/sex **Dose level:** Analytical concentration: 5.0 mg/L (mass median aerodynamic diameter = 4.07 µm; GSD = 2.37)	LC$_{50}$ > 5.0 mg/L	No mortalities and no treatment-related clinical observations, necropsy findings or changes in bw **LOW TOXICITY**
Eye irritation	NZW rabbits 3 rabbits/sex **Dose level:** 0.1 g	MIS: 2.67/110 at 1 h MAS (for 24, 48 and 72 h): 0.0/110	Very slight conjunctival redness and discharge in 3/6 animals and very slight chemosis in 2/6 animals at 1 h; resolved by 24 h **MINIMALLY IRRITATING**
Skin irritation	NZW rabbits 3 rabbits/sex **Dose level:** 0.5 g	MIS: 0.17/8 at 24, 48 and 72 h and at 7 days MAS (for 24, 48 and 72 h): 0.17/8	One rabbit developed very slight edema by 24 h; resolved by day 8 **MINIMALLY IRRITATING**
Skin sensitization (Buehler method)	Hartley albino guinea pigs 10 ♂ in treatment group and 5 ♂ in naive control group **Dose level:** 0.4 g XDE-570 moistened with 0.2 mL distilled water for induction and challenge treatments	No dermal reactions observed at any time after induction or challenge treatment	**NOT A DERMAL SENSITIZER**
Skin sensitization (Guinea pig Maximisation test of Magnusson and Kligman)	Dunkin/Hartley guinea pigs 20 ♂ in treatment group and 10 ♂ in naive control group **Dose levels:** Induction Intradermal: 1.0% w/v XDE-570 in Alembicol D Topical: 100% w/v XDE-570 in Alembicol D Challenge: 100 and 50% w/v XDE-570 in Alembicol D	No dermal reactions observed at 24 or 48 h after challenge treatment	**NOT A DERMAL SENSITIZER**

STUDY	SPECIES OR STRAIN AND DOSES	LD_{50}, LC_{50}, MIS OR MAS	TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS
ACUTE STUDIES: Formulation DE-570 g/L SC Herbicide (EF-1343)			
Oral: Limit test	CD-1 mice 5 mice/sex **Dose level:** 5000 mg/kg bw	LD_{50} greater than 5000 mg/kg bw in both sexes	No mortalities and no treatment-related clinical observations, necropsy findings or changes in bw **LOW TOXICITY**
Oral: Limit test	Fischer 344 rats 5 rats/sex **Dose level:** 5000 mg/kg bw	LD_{50} greater than 5000 mg/kg bw in both sexes	No mortalities and no treatment-related clinical observations, necropsy findings or changes in bw **LOW TOXICITY**
Oral: Limit test	CD (remote Sprague-Dawley origin) rats 5 rats/sex **Dose level:** 2000 mg/kg bw	LD_{50} greater than 2000 mg/kg bw in both sexes	No mortalities and no treatment-related clinical observations, necropsy findings or changes in bw **LOW TOXICITY**
Dermal: Limit test	CD strain rats (remote Sprague-Dawley) 5 rats/sex **Dose level:** 2000 mg/kg bw	LD_{50} greater than 2000 mg/kg bw in both sexes	No mortalities and no treatment-related clinical observations, necropsy findings or changes in bw **LOW TOXICITY**
Inhalation	A waiver in lieu of conducting an acute inhalation study was requested. The formulation is a liquid formulation. The vapour pressure of the technical grade active ingredient, DE-570, is 1×10^{-5} Pa at 25°C. The formulation is to be applied to cereals by field crop sprayers that do not generate a significant proportion (greater than 1% on a weight basis) of particles or droplets of diameter less than 50 µm. This waiver request is acceptable. The formulations are expected to have low toxicity via the acute inhalation route of exposure.		
Eye irritation	Outbred strain of NZW rabbits 3 ♀ **Dose level:** 0.1 mL of undiluted test substance	MIS: 2.0/110 at 1 h MAS (for 24, 48 and 72 h): 0.22/110	Minimal conjunctival redness in 3/3 animals; resolved by 48 h **MINIMALLY IRRITATING**
Eye irritation	Outbred strain of NZW rabbits 3 rabbits/sex **Dose level:** 0.1 mL of undiluted test substance	MIS: 2.0/110 at 1 h MAS (for 24, 48 and 72 h): 0.11/110	Slight conjunctival redness 5/6 animals and slight chemosis in 1/6 animals at 1 h, resolved by 48 h **MINIMALLY IRRITATING**
Skin irritation	CD strain rats (remote Sprague-Dawley) 5 rats/sex **Dose level:** 2000 mg/kg bw	MIS: 0/8 MAS (for 24, 48 and 72 h): 0/8	No dermal irritation observed at any time **NON-IRRITATING**
Skin sensitization (Modified Buehler method)	Dunkin Hartley albino guinea pigs 10 animals/sex in treatment group and 5 animals/sex in naive control group **Dose level:** 0.5 mL undiluted test substance for induction treatments (9) and challenge treatment (1).	No dermal reactions observed at any time after induction or challenge treatment	**NOT A DERMAL SENSITIZER**

STUDY	SPECIES OR STRAIN AND DOSES	LD_{50}, LC_{50}, MIS OR MAS	TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS
Oral	Fischer 344 rats 5 rats/sex/dose **Dose levels:** 1000, 3000 or 6000 mg/kg bw	LD_{50} greater than 6000 mg/kg bw for both sexes	No mortalities at 1000 or 3000 mg/kg bw. At 6000 mg/kg bw, 1 male (d 7) and 2 ♀ (d 2 and d 7) died (bw loss prior to death). No treatment-related clinical observations, necropsy findings or changes in bw **LOW TOXICITY**
Dermal: Limit test	New Zealand white (NZW) rabbits 5 rabbits/sex **Dose level:** 2000 mg/kg bw	LD_{50} greater than 2000 mg/kg bw for both sexes	No mortalities and no treatment-related clinical observations, necropsy findings or changes in bw **LOW TOXICITY**
Inhalation: Limit test (4-h nose-only)	Fischer 344 rats 5 rats/sex **Dose level:** Analytical concentration: 5.0 mg/L (mass median aerodynamic diameter = 4.07 µm; GSD = 2.37)	$LC_{50} > 5.0$ mg/L	No mortalities and no treatment-related clinical observations, necropsy findings or changes in bw **LOW TOXICITY**
Eye irritation	NZW rabbits 3 rabbits/sex **Dose level:** 0.1 g	MIS: 2.67/110 at 1 h MAS (for 24, 48 and 72 h): 0.0/110	Very slight conjunctival redness and discharge in 3/6 animals and very slight chemosis in 2/6 animals at 1 h; resolved by 24 h **MINIMALLY IRRITATING**
Skin irritation	NZW rabbits 3 rabbits/sex **Dose level:** 0.5 g	MIS: 0.17/8 at 24, 48 and 72 h and at 7 days MAS (for 24, 48 and 72 h): 0.17/8	One rabbit developed very slight edema by 24 h; resolved by day 8 **MINIMALLY IRRITATING**
Skin sensitization (Buehler method)	Hartley albino guinea pigs 10 ♂ in treatment group and 5 ♂ in naive control group **Dose level:** 0.4 g XDE-570 moistened with 0.2 mL distilled water for induction and challenge treatments	No dermal reactions observed at any time after induction or challenge treatment	**NOT A DERMAL SENSITIZER**
Skin sensitization (Guinea pig Maximisation test of Magnusson and Kligman)	Dunkin/Hartley guinea pigs 20 ♂ in treatment group and 10 ♂ in naive control group **Dose levels:** Induction Intradermal: 1.0% w/v XDE-570 in Alembicol D Topical: 100% w/v XDE-570 in Alembicol D Challenge: 100 and 50% w/v XDE-570 in Alembicol D	No dermal reactions observed at 24 or 48 h after challenge treatment	**NOT A DERMAL SENSITIZER**

STUDY	SPECIES OR STRAIN AND DOSES	LD_{50}, LC_{50}, MIS OR MAS	TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS
ACUTE STUDIES: Formulation DE-570 g/L SC Herbicide (EF-1343)			
Oral: Limit test	CD-1 mice 5 mice/sex **Dose level:** 5000 mg/kg bw	LD_{50} greater than 5000 mg/kg bw in both sexes	No mortalities and no treatment-related clinical observations, necropsy findings or changes in bw **LOW TOXICITY**
Oral: Limit test	Fischer 344 rats 5 rats/sex **Dose level:** 5000 mg/kg bw	LD_{50} greater than 5000 mg/kg bw in both sexes	No mortalities and no treatment-related clinical observations, necropsy findings or changes in bw **LOW TOXICITY**
Oral: Limit test	CD (remote Sprague-Dawley origin) rats 5 rats/sex **Dose level:** 2000 mg/kg bw	LD_{50} greater than 2000 mg/kg bw in both sexes	No mortalities and no treatment-related clinical observations, necropsy findings or changes in bw **LOW TOXICITY**
Dermal: Limit test	CD strain rats (remote Sprague-Dawley) 5 rats/sex **Dose level:** 2000 mg/kg bw	LD_{50} greater than 2000 mg/kg bw in both sexes	No mortalities and no treatment-related clinical observations, necropsy findings or changes in bw **LOW TOXICITY**
Inhalation	A waiver in lieu of conducting an acute inhalation study was requested. The formulation is a liquid formulation. The vapour pressure of the technical grade active ingredient, DE-570, is 1×10^{-5} Pa at 25°C. The formulation is to be applied to cereals by field crop sprayers that do not generate a significant proportion (greater than 1% on a weight basis) of particles or droplets of diameter less than 50 µm. This waiver request is acceptable. The formulations are expected to have low toxicity via the acute inhalation route of exposure.		
Eye irritation	Outbred strain of NZW rabbits 3 ♀ **Dose level:** 0.1 mL of undiluted test substance	MIS: 2.0/110 at 1 h MAS (for 24, 48 and 72 h): 0.22/110	Minimal conjunctival redness in 3/3 animals; resolved by 48 h **MINIMALLY IRRITATING**
Eye irritation	Outbred strain of NZW rabbits 3 rabbits/sex **Dose level:** 0.1 mL of undiluted test substance	MIS: 2.0/110 at 1 h MAS (for 24, 48 and 72 h): 0.11/110	Slight conjunctival redness 5/6 animals and slight chemosis in 1/6 animals at 1 h, resolved by 48 h **MINIMALLY IRRITATING**
Skin irritation	CD strain rats (remote Sprague-Dawley) 5 rats/sex **Dose level:** 2000 mg/kg bw	MIS: 0/8 MAS (for 24, 48 and 72 h): 0/8	No dermal irritation observed at any time **NON-IRRITATING**
Skin sensitization (Modified Buehler method)	Dunkin Hartley albino guinea pigs 10 animals/sex in treatment group and 5 animals/sex in naive control group **Dose level:** 0.5 mL undiluted test substance for induction treatments (9) and challenge treatment (1)	No dermal reactions observed at any time after induction or challenge treatment	**NOT A DERMAL SENSITIZER**

STUDY	SPECIES OR STRAIN AND DOSES	NOAEL AND LOAEL (mg/kg bw/d)	TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS
SHORT TERM: Technical florasulam (XDE-570)			
90-d dietary: mouse	10 $B6C3F_1$ mice/sex/dose **Dose level:** 0, 20, 100, 500 or 1000 mg/kg bw/d	**NOAEL:** 100 mg/kg bw/d **LOAEL:** 500 mg/kg bw/d	500 mg/kg bw/d: hypertrophy epithelial cells collecting ducts (♂) 1000 mg/kg bw/d: hypertrophy epithelial cells collecting ducts (both sexes) **Control week 13 bw** ♂: 31.4 g ♀: 25.6 g **Control week 13 daily food consumption** ♂: 6.0 g/animal ♀: 6.4 g/animal
90-d dietary (with 4-week recovery): rat	10 Fischer 344 rats/sex/dose **Dose levels:** 0, 20, 100, 500, 800 (♀ only) or 1000 (♂ only) mg/kg bw/d	**NOAEL:** 100 mg/kg bw/d **LOAEL:** 500 mg/kg bw/d	500 mg/kg bw/d and above: lower bw and bwg (♀); marginal ↓ red blood cell (RBC) counts, hemoglobin (HGB) and hematocrit (HCT) (♂); urinary acidification (♂ and ♀); ↑ kidney weight (♂ and ♀); hypertrophy epithelial cells collecting ducts (♂ and ♀); degeneration and regeneration descending portion proximal tubules (♀) 800 mg/kg bw/d (♀ only): lower food consumption; multi-focal mineralization renal papilla 1000 mg/kg bw/d (♂ only): lower bw, bwg and food consumption; ↓ urinary SG **Control week 13 bw** ♂: 316 g ♀: 180 g **Control week 13 daily food consumption** ♂: 18.6 g/animal ♀: 12.0 g/animal
90-d dietary: dog	4 dogs/sex/dose (Beagle) **Dose levels:** 0, 5, 50 or 100 mg/kg bw/d	**NOAEL:** 5 mg/kg bw/d **LOAEL:** 50 mg/kg bw/d	50 mg/kg bw/d and above: ↑ ALP (♂ and ♀); ↑ incidence/severity hepatic vacuolation (♂ and ♀); hypertrophy epithelial cells collecting ducts (♂ and ♀). 100 mg/kg bw/d: ↑ liver weight (♂ and ♀)

STUDY	SPECIES OR STRAIN AND DOSES	NOAEL AND LOAEL (mg/kg bw/d)	TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS
12-month dietary: dog	4 dogs/sex/dose (Beagle) **Dose levels:** 0, 0.5, 5 or 100/50* mg/kg bw/d * Due to bw loss and lower food consumption at 100 mg/kg bw/d (♂ and ♀) during the first 3 months of the study (up to study day 104), the HD level was decreased to 50 mg/kg bw/d (beginning study day 105) for reasons of animal welfare.	**NOAEL:** 5 mg/kg bw/d **LOAEL:** 50 mg/kg bw/d	Findings at 100 mg/kg bw/d, prior to decreasing HD to 50 mg/kg bw/d: lower bw, bwg and food consumption (♂ and ♀); ↑ ALAT and ALP and ↓ albumin and protein (♂ and ♀) 50 mg/kg bw/d (beginning day 105): lower bw, bwg and food consumption (♀); ↑ ALP and ↓ albumin and protein (♂ and ♀); ↑ severity hypertrophy epithelial cells collecting ducts (♂ and ♀); slight vacuolization zona reticularis and zona fasciculata adrenal gland, toxicological significance uncertain (♂ and ♀)
4-week dermal: rat	5 Fischer 344 rats/sex/dose **Dose levels:** 0, 100, 500 or 1000 mg/kg bw/d	**Systemic** NOAEL: 1000 mg/kg bw/d LOAEL: Not determined	No treatment-related systemic findings in either sex **Local irritation:** Slight transient erythema and edema at application site (♂ at 1000 mg/kg bw/d)
CHRONIC TOXICITY OR ONCOGENICITY: Technical florasulam (XDE-570)			
two-year dietary: mouse	60 B6C3F$_1$ mice/sex/dose (10/sex/dose sacrifice at 1 year and 50/sex/dose sacrifice at 2 years) **Dose levels:** 0, 50, 500 or 1000 mg/kg bw/d	**Chronic toxicity** NOAEL: 50 mg/kg bw/d LOAEL: 500 mg/kg bw/d	500 mg/kg bw/d and above: ↓ kidney weight (♂, no clear dose–response relationship); ↓ cytoplasmic vacuolation cortical tubular epithelium cells (♂); hypertrophy epithelial cells collecting ducts (♂ and ♀); ↓ incidence (♀) or severity (♂) of age-related tubular degeneration with regeneration No evidence to indicate any carcinogenic potential of florasulam up to and including 1000 mg/kg bw/d (HDT)

STUDY	SPECIES OR STRAIN AND DOSES	NOAEL AND LOAEL (mg/kg bw/d)	TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS
SHORT TERM: Technical florasulam (XDE-570)			
90-d dietary: mouse	10 B6C3F$_1$ mice/sex/dose **Dose level:** 0, 20, 100, 500 or 1000 mg/kg bw/d	**NOAEL:** 100 mg/kg bw/d **LOAEL:** 500 mg/kg bw/d	500 mg/kg bw/d: hypertrophy epithelial cells collecting ducts (♂) 1000 mg/kg bw/d: hypertrophy epithelial cells collecting ducts (both sexes) **Control week 13 bw** ♂: 31.4 g ♀: 25.6 g **Control week 13 daily food consumption** ♂: 6.0 g/animal ♀: 6.4 g/animal
90-d dietary (with 4-week recovery): rat	10 Fischer 344 rats/sex/dose **Dose levels:** 0, 20, 100, 500, 800 (♀ only) or 1000 (♂ only) mg/kg bw/d	**NOAEL:** 100 mg/kg bw/d **LOAEL:** 500 mg/kg bw/d	500 mg/kg bw/d and above: lower bw and bwg (♀); marginal ↓ red blood cell (RBC) counts, hemoglobin (HGB) and hematocrit (HCT) (♂); urinary acidification (♂ and ♀); ↑ kidney weight (♂ and ♀); hypertrophy epithelial cells collecting ducts (♂ and ♀); degeneration and regeneration descending portion proximal tubules (♀) 800 mg/kg bw/d (♀ only): lower food consumption; multi-focal mineralization renal papilla 1000 mg/kg bw/d (♂ only): lower bw, bwg and food consumption; ↓ urinary SG **Control week 13 bw** ♂: 316 g ♀: 180 g **Control week 13 daily food consumption** ♂: 18.6 g/animal ♀: 12.0 g/animal
90-d dietary: dog	4 dogs/sex/dose (Beagle) **Dose levels:** 0, 5, 50 or 100 mg/kg bw/d	**NOAEL:** 5 mg/kg bw/d **LOAEL:** 50 mg/kg bw/d	50 mg/kg bw/d and above: ↑ ALP (♂ and ♀); ↑ incidence/severity hepatic vacuolation (♂ and ♀); hypertrophy epithelial cells collecting ducts (♂ and ♀). 100 mg/kg bw/d: ↑ liver weight (♂ and ♀)

STUDY	SPECIES OR STRAIN AND DOSES	NOAEL AND LOAEL (mg/kg bw/d)	TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS
12-month dietary: dog	4 dogs/sex/dose (Beagle) **Dose levels:** 0, 0.5, 5 or 100/50* mg/kg bw/d * Due to bw loss and lower food consumption at 100 mg/kg bw/d (♂ and ♀) during the first 3 months of the study (up to study day 104), the HD level was decreased to 50 mg/kg bw/d (beginning study day 105) for reasons of animal welfare.	**NOAEL:** 5 mg/kg bw/d **LOAEL:** 50 mg/kg bw/d	Findings at 100 mg/kg bw/d, prior to decreasing HD to 50 mg/kg bw/d: lower bw, bwg and food consumption (♂ and ♀); ↑ ALAT and ALP and ↓ albumin and protein (♂ and ♀) 50 mg/kg bw/d (beginning day 105): lower bw, bwg and food consumption (♀); ↑ ALP and ↓ albumin and protein (♂ and ♀); ↑ severity hypertrophy epithelial cells collecting ducts (♂ and ♀); slight vacuolization zona reticularis and zona fasciculata adrenal gland, toxicological significance uncertain (♂ and ♀)
4-week dermal: rat	5 Fischer 344 rats/sex/dose **Dose levels:** 0, 100, 500 or 1000 mg/kg bw/d	**Systemic** NOAEL: 1000 mg/kg bw/d LOAEL: Not determined	No treatment-related systemic findings in either sex **Local irritation:** Slight transient erythema and edema at application site (♂ at 1000 mg/kg bw/d)
CHRONIC TOXICITY OR ONCOGENICITY: Technical florasulam (XDE-570)			
two-year dietary: mouse	60 B6C3F$_1$ mice/sex/dose (10/sex/dose sacrifice at 1 year and 50/sex/dose sacrifice at 2 years) **Dose levels:** 0, 50, 500 or 1000 mg/kg bw/d	**Chronic toxicity** NOAEL: 50 mg/kg bw/d LOAEL: 500 mg/kg bw/d	500 mg/kg bw/d and above: ↓ kidney weight (♂, no clear dose–response relationship); ↑ cytoplasmic vacuolation cortical tubular epithelium cells (♂); hypertrophy epithelial cells collecting ducts (♂ and ♀); ↓ incidence (♀) or severity (♂) of age-related tubular degeneration with regeneration No evidence to indicate any carcinogenic potential of florasulam up to and including 1000 mg/kg bw/d (HDT)

STUDY	SPECIES OR STRAIN AND DOSES	NOAEL AND LOAEL (mg/kg bw/d)	TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS
two-year dietary: rat	60 Fischer 344 rats/sex/dose (10 rats/sex/dose interim sacrifice + 50 rats/sex/dose terminal sacrifice) **Dose levels:** 0, 10, 125 (♀ only), 250 or 500 (♂ only) mg/kg bw/d	**Chronic toxicity** NOAEL: 10 mg/kg bw/d LOAEL: 125 mg/kg bw/d	125 mg/kg bw/d (♀ only): marginal to slight ↑ kidney weight; equivocal urinary acidification; hypertrophy epithelial cells collecting duct 250 mg/kg bw/d: lower bw, bwg and food consumption (♀); urinary acidification (♂ and ♀); ↑ kidney weight (♂ and ♀); hypertrophy epithelial cells collecting duct (♂ and ♀); ↓ incidence age-related tubular degeneration and regeneration (♂); ↓ severity (♂) and incidence (♀) geriatric renal degeneration (chronic progressive glomerularnephropathy) 500 mg/kg bw/d (♂ only): lower bw, bwg and food consumption; ↓ RBC counts, HGB and HCT, reversed by 24 months; ↑ serum bicarbonate; urinary acidification, ↓ urinary SG and proteinuria; ↑ kidney weight; hypertrophy epithelial cells collecting duct; ↓ incidence age-related tubular degeneration or regeneration; ↓ severity geriatric renal degeneration (chronic progressive glomerularnephropathy); minimal reactive hyperplasia transitional epithelium; unilateral necrosis papilla No evidence to indicate any carcinogenic potential of florasulam up to and including 250 mg/kg bw/d, HDT in ♀ and up to and including 500 mg/kg bw/d, HDT in ♂

STUDY	SPECIES OR STRAIN AND DOSES	NOAEL AND LOAEL (mg/kg bw/d)	TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS
REPRODUCTION AND DEVELOPMENTAL TOXICITY: Technical florasulam (XDE-570)			
Multi-generation: rat (1 litter/generation)	30 CD (Sprague-Dawley derived) rats/sex/group **Dose levels:** 0, 10, 100 or 500 mg/kg bw/d	**Parental** NOAEL: 100 mg/kg bw/d LOAEL: 500 mg/kg bw/d **Offspring** NOAEL: 100 mg/kg bw/d LOAEL: 500 mg/kg bw/d **Reproductive** NOAEL: 500 mg/kg bw/d LOAEL: Not determined	**Parental** 500 mg/kg bw/d: lower bw, bwg and food consumption P_2 ♂ and P_1/P_2 ♀; ↑ kidney weight (P_2 ♂ and P_1/P_2 ♀); hypertrophy epithelial cells collecting duct (P_1/P_2 both sexes) **Offspring** 500 mg/kg bw/d: transient lower bw on lactation days 4 and 7, comparable to control by lactation day 14 (F_1/F_2 both sexes), possibly secondary to lower maternal food consumption early in lactation period **Reproductive** No adverse treatment-related effects on reproductive parameters up to and including 500 mg/kg bw/d (HDT)
Developmental: rat	25–27 sexually mature female CD (Sprague-Dawley) rats/dose **Dose levels:** 0, 50, 250 or 750 mg/kg bw/d	**Maternal toxicity:** NOAEL: 250 mg/kg bw/d LOAEL: 750 mg/kg bw/d **Developmental toxicity:** NOAEL: 750 mg/kg bw/d LOAEL: not determined	**Maternal toxicity:** 750 mg/kg bw/d: lower bw, bwg and food consumption; ↑ kidney weight (no corroborating gross pathological findings, no histopathology done, toxicological significance uncertain); 4 mortalities at 750 mg/kg bw/d, 3 deaths were attributed to gavage error, cause of the 4th death not determined, treatment-related cause not excluded; dams pregnant with normally developing fetuses **Developmental toxicity:** No significant treatment-related findings at any dose level up to and including 750 mg/kg bw/d (HDT) **Teratogenicity:** No evidence of any treatment-related irreversible structural changes at any dose level up to and including 750 mg/kg bw/d (HDT); therefore, under the conditions of the study, florasulam was not teratogenic.

STUDY	SPECIES OR STRAIN AND DOSES	NOAEL AND LOAEL (mg/kg bw/d)	TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS
two-year dietary: rat	60 Fischer 344 rats/sex/dose (10 rats/sex/dose interim sacrifice + 50 rats/sex/dose terminal sacrifice) **Dose levels:** 0, 10, 125 (♀ only), 250 or 500 (♂ only) mg/kg bw/d	**Chronic toxicity** NOAEL: 10 mg/kg bw/d LOAEL: 125 mg/kg bw/d	125 mg/kg bw/d (♀ only): marginal to slight ↑ kidney weight; equivocal urinary acidification; hypertrophy epithelial cells collecting duct 250 mg/kg bw/d: lower bw, bwg and food consumption (♀); urinary acidification (♂ and ♀); ↑ kidney weight (♂ and ♀); hypertrophy epithelial cells collecting duct (♂ and ♀); ↓ incidence age-related tubular degeneration and regeneration (♂); ↓ severity (♂) and incidence (♀) geriatric renal degeneration (chronic progressive glomerularnephropathy) 500 mg/kg bw/d (♂ only): lower bw, bwg and food consumption; ↓ RBC counts, HGB and HCT, reversed by 24 months; ↑ serum bicarbonate; urinary acidification, ↓ urinary SG and proteinuria; ↑ kidney weight; hypertrophy epithelial cells collecting duct; ↓ incidence age-related tubular degeneration or regeneration; ↓ severity geriatric renal degeneration (chronic progressive glomerularnephropathy); minimal reactive hyperplasia transitional epithelium; unilateral necrosis papilla No evidence to indicate any carcinogenic potential of florasulam up to and including 250 mg/kg bw/d, HDT in ♀ and up to and including 500 mg/kg bw/d, HDT in ♂

STUDY	SPECIES OR STRAIN AND DOSES	NOAEL AND LOAEL (mg/kg bw/d)	TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS
REPRODUCTION AND DEVELOPMENTAL TOXICITY: Technical florasulam (XDE-570)			
Multi-generation: rat (1 litter/generation)	30 CD (Sprague-Dawley derived) rats/sex/group **Dose levels:** 0, 10, 100 or 500 mg/kg bw/d	**Parental** NOAEL: 100 mg/kg bw/d LOAEL: 500 mg/kg bw/d **Offspring** NOAEL: 100 mg/kg bw/d LOAEL: 500 mg/kg bw/d **Reproductive** NOAEL: 500 mg/kg bw/d LOAEL: Not determined	**Parental** 500 mg/kg bw/d: lower bw, bwg and food consumption P_2 ♂ and P_1/P_2 ♀; ↑ kidney weight (P_2 ♂ and P_1/P_2 ♀); hypertrophy epithelial cells collecting duct (P_1/P_2 both sexes) **Offspring** 500 mg/kg bw/d: transient lower bw on lactation days 4 and 7, comparable to control by lactation day 14 (F_1/F_2 both sexes), possibly secondary to lower maternal food consumption early in lactation period **Reproductive** No adverse treatment-related effects on reproductive parameters up to and including 500 mg/kg bw/d (HDT)
Developmental: rat	25–27 sexually mature female CD (Sprague-Dawley) rats/dose **Dose levels:** 0, 50, 250 or 750 mg/kg bw/d	**Maternal toxicity:** NOAEL: 250 mg/kg bw/d LOAEL: 750 mg/kg bw/d **Developmental toxicity:** NOAEL: 750 mg/kg bw/d LOAEL: not determined	**Maternal toxicity:** 750 mg/kg bw/d: lower bw, bwg and food consumption, ↑ kidney weight (no corroborating gross pathological findings, no histopathology done, toxicological significance uncertain); 4 mortalities at 750 mg/kg bw/d, 3 deaths were attributed to gavage error, cause of the 4th death not determined, treatment-related cause not excluded; dams pregnant with normally developing fetuses **Developmental toxicity:** No significant treatment-related findings at any dose level up to and including 750 mg/kg bw/d (HDT) **Teratogenicity:** No evidence of any treatment-related irreversible structural changes at any dose level up to and including 750 mg/kg bw/d (HDT); therefore, under the conditions of the study, florasulam was not teratogenic

STUDY	SPECIES OR STRAIN AND DOSES	NOAEL AND LOAEL (mg/kg bw/d)	TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS
Preliminary developmental: rabbit	7 sexually mature female NZW rabbits/dose **Dose levels:** 0, 100, 300, 600 or 1000 mg/kg bw/d	**Maternal toxicity** NOAEL: 300 mg/kg bw/d LOAEL: 600 mg/kg bw/d **Developmental toxicity** NOAEL: not determined LOAEL: not determined	**Maternal toxicity:** 600 mg/kg bw/d: 1 death (14%) with severe bw loss, markedly lower food consumption and fecal output prior to death; remaining dams exhibited bw loss (food consumption unaffected) during gestation days 7–10; lower bwg and food consumption during remainder of gestation 1000 mg/kg bw/d: 3 deaths (43%) with severe bw loss, markedly lower food consumption and fecal output prior to death; remaining dams lower bwg and food consumption; euthanized on gestation day 17 **Developmental toxicity:** No fetal evaluation; dams sacrificed on gestation day 20 **Teratogenicity:** No fetal evaluation; dams sacrificed on gestation day 20
Developmental: rabbit	20 sexually mature female NZW rabbits/dose **Dose levels:** 0, 50, 250 or 500 mg/kg bw/d	**Maternal toxicity** NOAEL: >500 mg/kg bw/d LOAEL: not determined **Developmental toxicity** NOAEL: >500 mg/kg bw/d LOAEL: not determined	**Maternal toxicity:** No treatment-related findings at any dose level up to and including 500 mg/kg bw/d (HDT) **Developmental toxicity:** No treatment-related findings at any dose level up to and including, 500 mg/kg bw/d (HDT) **Teratogenicity:** No evidence of any treatment-related irreversible structural changes at any dose level up to and including 500 mg/kg bw/d (HDT); therefore, under the conditions of the study, florasulam was not teratogenic.
STUDY	**SPECIES OR STRAIN OR CELL TYPE**	**DOSE LEVELS**	**SIGNIFICANT EFFECTS AND COMMENTS**
GENOTOXICITY: Technical florasulam (XDE-570)			
Salmonella/Ames Test/*Escherichia coli* bacterial mutation assay	*Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537 and *E. coli* strain WP$_2$*uvr*A	0, 0.333, 1.00, 3.33, 10, 33.3 or 100 μg/plate for *S. typhimurium* and 0, 10, 33.3, 100, 333, 1000 or 3330 μg/plate for *E. coli* ± S9 metabolic activation	**Negative** for both *S. typhimurium* and *E. coli* tester strains
Mammalian chromosomal aberration (in vitro)	Chinese hamster ovary cells (at the HGPRT locus)	0, 187.5, 375, 750 or 3000 μg/mL ± S9 metabolic activation.	**Negative**
Mammalian cytogenetics (in vitro)	Primary rat lymphocytes	0, 3, 10, 30, 100, 300, 1000 or 3000 μg/mL ± S9 metabolic activation	**Negative**
Micronucleus assay (in vivo)	Male and female mouse bone marrow cells (erythrocytes)	0, 1250, 2500 or 5000 mg/kg bw	**Negative**

STUDY	SPECIES OR STRAIN AND DOSES	NOAEL AND LOAEL (mg/kg bw/d)	TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS
SPECIAL STUDIES: Technical florasulam (XDE-570)			
Acute neurotoxicity screening battery: rat	10 young-adult Fischer 344 rats/sex/dose **Dose levels:** 0, 200, 1000 or 2000 mg/kg bw	**Systemic** NOAEL: 1000 mg/kg bw LOAEL: 2000 mg/kg bw **Neurotoxicity** NOAEL: 2000 mg/kg bw LOAEL: Not determined	**Systemic toxicity** 2000 mg/kg bw: lower bwg (♂); slight transient ↓ motor activity, ↑ incidence of minimal level of activity in open field and ↑ incidence of minimal responsiveness to sharp noise on day of dosing (♂); suggest slight transient depression of activity and reactivity on day of dosing; probably due to general malaise and not to neurotoxicity per se **Neurotoxicity** No evidence of neurotoxicity in either sex up to and including 2000 mg/kg bw (limit dose)
Chronic neurotoxicity screening battery: rat	10 young-adult Fischer 344 rats/sex/dose **Dose levels**: 0, 10, 125 (♀ only), 250 or 500 (♂ only) mg/kg bw/d	**Systemic** NOAEL: 250 mg/kg bw/d LOAEL: 500 mg/kg bw/d **Neurotoxicity** NOAEL: 250 mg/kg bw/d LOAEL: Not determined	**Systemic toxicity** 500 mg/kg bw/d: lower bw and bwg (♂) **Neurotoxicity**: No evidence of neurotoxicity in either sex up to and including 500 mg/kg bw/d (♂ HDT) and 250 mg/kg bw/d (♀ HDT)
SPECIAL STUDIES: Formulation DE-570 g/L SC Herbicide (EF-1343)			
4-week dermal: rat EUP: EF-1343 (XDE-570 50 SC)	5 young adult Fischer 344 rats/sex/dose **Dose levels:** 0, 100, 500 or 1000 mg/kg bw/d	**Systemic** NOAEL: 1000 mg/kg bw/d LOAEL: Not determined	No treatment-related systemic findings in either sex at any dose level up to and including 1000 mg/kg bw/d (HDT) No signs of dermal irritation at the dermal application site in any control or treatment groups animal

Compound-induced mortality: There was no significant increased incidence of treatment-related mortalities in any short-term, long-term or special studies. However, in a rat developmental study, there were 4 mortalities (4/27, ~15%) at 750 mg/kg bw/d (HDT), 3 deaths were attributed to gavage error, cause of the 4th death not determined although treatment-related cause was not excluded. In a rabbit preliminary developmental study, mortalities were observed at 600 (1/7, ~14%) and 1000 mg/kg bw/d (3/7, ~43%), all of these dams exhibited severe bw loss, markedly lower food consumption and decreased fecal output prior to death. All of these dams were pregnant with normally developing fetuses. These deaths were considered to be treatment-related, however, possibility of gavage error could not be eliminated as possible cause of death since the dam at 600 mg/kg bw/d and 2 dams at 1000 mg/kg bw/d exhibited edematous lungs. There were no treatment-related deaths in the main rabbit developmental toxicity study at any dose level up to and including 500 mg/kg bw/d (HDT).

Recommended ARfD: An ARfD was not established, since florasulam was considered unlikely to present an acute hazard. There were no significant treatment-related findings in the acute, short-term, two-generation reproduction or developmental toxicity studies or in the acute or subchronic neurotoxicity studies to indicate a concern in acute dietary risk assessment.

STUDY	SPECIES OR STRAIN AND DOSES	NOAEL AND LOAEL (mg/kg bw/d)	TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS
Preliminary developmental: rabbit	7 sexually mature female NZW rabbits/dose **Dose levels:** 0, 100, 300, 600 or 1000 mg/kg bw/d	**Maternal toxicity** NOAEL: 300 mg/kg bw/d LOAEL: 600 mg/kg bw/d **Developmental toxicity** NOAEL: not determined LOAEL: not determined	**Maternal toxicity:** 600 mg/kg bw/d: 1 death (14%) with severe bw loss, markedly lower food consumption and fecal output prior to death; remaining dams exhibited bw loss (food consumption unaffected) during gestation days 7–10; lower bwg and food consumption during remainder of gestation 1000 mg/kg bw/d: 3 deaths (43%) with severe bw loss, markedly lower food consumption and fecal output prior to death; remaining dams lower bwg and food consumption; euthanized on gestation day 17 **Developmental toxicity:** No fetal evaluation; dams sacrificed on gestation day 20 **Teratogenicity:** No fetal evaluation; dams sacrificed on gestation day 20
Developmental rabbit	20 sexually mature female NZW rabbits/dose **Dose levels:** 0, 50, 250 or 500 mg/kg bw/d	**Maternal toxicity** NOAEL: >500 mg/kg bw/d LOAEL: not determined **Developmental toxicity** NOAEL: >500 mg/kg bw/d LOAEL: not determined	**Maternal toxicity:** No treatment-related findings at any dose level up to and including 500 mg/kg bw/d (HDT) **Developmental toxicity:** No treatment-related findings at any dose level up to and including, 500 mg/kg bw/d (HDT) **Teratogenicity:** No evidence of any treatment-related irreversible structural changes at any dose level up to and including 500 mg/kg bw/d (HDT); therefore, under the conditions of the study, florasulam was not teratogenic.

STUDY	SPECIES OR STRAIN OR CELL TYPE	DOSE LEVELS	SIGNIFICANT EFFECTS AND COMMENTS
GENOTOXICITY: Technical florasulam (XDE-570)			
Salmonella/Ames Test/*Escherichia coli* bacterial mutation assay	*Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537 and *E. coli* strain WP$_2$*uvr*A	0, 0.333, 1.00, 3.33, 10, 33.3 or 100 µg/plate for *S. typhimurium* and 0, 10, 33.3, 100, 333, 1000 or 3330 µg/plate for *E. coli* ± S9 metabolic activation	**Negative** for both *S. typhimurium* and *E. coli* tester strains
Mammalian chromosomal aberration (in vitro)	Chinese hamster ovary cells (at the HGPRT locus)	0, 187.5, 375, 750 or 3000 µg/mL ± S9 metabolic activation.	**Negative**
Mammalian cytogenetics (in vitro)	Primary rat lymphocytes	0, 3, 10, 30, 100, 300, 1000 or 3000 µg/mL ± S9 metabolic activation	**Negative**
Micronucleus assay (in vivo)	Male and female mouse bone marrow cells (erythrocytes)	0, 1250, 2500 or 5000 mg/kg bw	**Negative**

STUDY	SPECIES OR STRAIN AND DOSES	NOAEL AND LOAEL (mg/kg bw/d)	TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS
SPECIAL STUDIES: Technical florasulam (XDE-570)			
Acute neurotoxicity screening battery: rat	10 young-adult Fischer 344 rats/sex/dose **Dose levels:** 0, 200, 1000 or 2000 mg/kg bw	**Systemic** NOAEL: 1000 mg/kg bw LOAEL: 2000 mg/kg bw **Neurotoxicity** NOAEL: 2000 mg/kg bw LOAEL: Not determined	**Systemic toxicity** 2000 mg/kg bw: lower bwg (♂); slight transient ↓ motor activity, ↑ incidence of minimal level of activity in open field and ↑ incidence of minimal responsiveness to sharp noise on day of dosing (♂); suggest slight transient depression of activity and reactivity on day of dosing; probably due to general malaise and not to neurotoxicity per se **Neurotoxicity** No evidence of neurotoxicity in either sex up to and including 2000 mg/kg bw (limit dose)
Chronic neurotoxicity screening battery: rat	10 young-adult Fischer 344 rats/sex/dose **Dose levels**: 0, 10, 125 (♀ only), 250 or 500 (♂ only) mg/kg bw/d	**Systemic** NOAEL: 250 mg/kg bw/d LOAEL: 500 mg/kg bw/d **Neurotoxicity** NOAEL: 250 mg/kg bw/d LOAEL: Not determined	**Systemic toxicity** 500 mg/kg bw/d: lower bw and bwg (♂) **Neurotoxicity**: No evidence of neurotoxicity in either sex up to and including 500 mg/kg bw/d (♂ HDT) and 250 mg/kg bw/d (♀ HDT)
SPECIAL STUDIES: Formulation DE-570 g/L SC Herbicide (EF-1343)			
4-week dermal: rat EUP: EF-1343 (XDE-570 50 SC)	5 young adult Fischer 344 rats/sex/dose **Dose levels:** 0, 100, 500 or 1000 mg/kg bw/d	**Systemic** NOAEL: 1000 mg/kg bw/d LOAEL: Not determined	No treatment-related systemic findings in either sex at any dose level up to and including 1000 mg/kg bw/d (HDT) No signs of dermal irritation at the dermal application site in any control or treatment groups animal
Compound-induced mortality: There was no significant increased incidence of treatment-related mortalities in any short-term, long-term or special studies. However, in a rat developmental study, there were 4 mortalities (4/27, ~15%) at 750 mg/kg bw/d (HDT), 3 deaths were attributed to gavage error, cause of the 4th death not determined although treatment-related cause was not excluded. In a rabbit preliminary developmental study, mortalities were observed at 600 (1/7, ~14%) and 1000 mg/kg bw/d (3/7, ~43%), all of these dams exhibited severe bw loss, markedly lower food consumption and decreased fecal output prior to death. All of these dams were pregnant with normally developing fetuses. These deaths were considered to be treatment-related, however, possibility of gavage error could not be eliminated as possible cause of death since the dam at 600 mg/kg bw/d and 2 dams at 1000 mg/kg bw/d exhibited edematous lungs. There were no treatment-related deaths in the main rabbit developmental toxicity study at any dose level up to and including 500 mg/kg bw/d (HDT).			
Recommended ARfD: An ARfD was not established, since florasulam was considered unlikely to present an acute hazard. There were no significant treatment-related findings in the acute, short-term, two-generation reproduction or developmental toxicity studies or in the acute or subchronic neurotoxicity studies to indicate a concern in acute dietary risk assessment.			

<table>
<tr><th>STUDY</th><th>SPECIES OR STRAIN AND DOSES</th><th>NOAEL AND LOAEL (mg/kg bw/d)</th><th>TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS</th></tr>
<tr><td colspan="4">Recommended ADI: The most appropriate NOAEL of 5.0 mg/kg bw/d in the one-year dietary study in dogs is recommended as the basis for the ADI. Treatment-related findings at the LOAEL (next highest dose level) included lower body weight, body-weight gain and food consumption (♀), increased ALP activity (both sexes) and decreased serum albumin and protein levels (both sexes) at 50 mg/kg bw/d and increased severity of hypertrophy of the epithelial cells of the collecting ducts and slight vacuolization of the zona reticularis and zona fasciculata in the adrenal glands in both sexes at 100 and 50 mg/kg bw/d. A safety factor of 100 to account for intra- and inter-species variations was applied to this NOAEL to determine the ADI. No additional safety factor is required. The recommended ADI is 0.05 mg/kg bw/d.

MOE for other critical end point(s): calculated as NOAEL/ADI
Developmental toxicity: NOAEL = 250 mg/kg bw/d (rat). The MOE for developmental toxicity is 5000 compared with the ADI.
Two-generation reproduction study:
Reproductive toxicity: NOAEL = 500 mg/kg bw/d. The MOE is 10 000 compared with the ADI
Offspring toxicity: NOAEL = 100 mg/kg bw/d. The MOE is 2000 compared with the ADI</td></tr>
</table>

Table 6 Residues

<table>
<tr><th colspan="7">Directions for use</th></tr>
<tr><th>Crop</th><th>Formulation type</th><th>Interval (days)</th><th>Rate (g a.i./ha)</th><th>Application/ season</th><th>Maximum rate (g a.i./ha)</th><th>PHI (days)</th></tr>
<tr><td>wheat (spring, durum), barley (spring), oat</td><td>EF-1343 Suspension concentrate (50 g/L)</td><td>postemergent 2-leaf crop up to and including the flag leaf extended stage</td><td>5</td><td>1</td><td>5</td><td>60</td></tr>
<tr><th colspan="7">Physicochemical properties</th></tr>
<tr><td colspan="2">Water solubility (g/L)</td><td colspan="5">0.121; 0.084 (pH 5); 6.36 (pH 7); 94.2 (pH 9)</td></tr>
<tr><td colspan="2">Solvent solubility (g/L)</td><td colspan="5">123.0 (acetone); 72.1 (acetonitrile); 15.9 (ethyl acetate); 9.81 (methanol); 3.75 (dichloromethane); 0.227 (xylene); 0.184 (<i>n</i>-octanol); 0.000019 (<i>n</i>-heptane)</td></tr>
<tr><td colspan="2"><i>n</i>-octanol–water partition coefficient (Log K_{ow})</td><td colspan="5">1.00 (pH 4); -1.22 (pH 7); -2.06 (pH 10)</td></tr>
<tr><td colspan="2">Dissociation constant (pK_a)</td><td colspan="5">4.54</td></tr>
<tr><td colspan="2">Vapour pressure (Pa)</td><td colspan="5">1 x 10^{-5}</td></tr>
<tr><td colspan="2">Melting point °C</td><td colspan="5">193.5–230.5</td></tr>
<tr><td colspan="2">UV-visible absorption spectrum</td><td colspan="5">No absorbance at $\lambda > 300$ nm.
203.8–259.8 (acidic medium); 209.7–262.4 (basic medium); 204.1 (methanolic)</td></tr>
<tr><th colspan="7">Analytical methodology</th></tr>
<tr><th>Parameters</th><th colspan="6">Plant matrices</th></tr>
<tr><td>Method ID</td><td colspan="2">GRM 98.01</td><td colspan="2">GRM 97.01</td><td colspan="2">GRM 99.17</td></tr>
<tr><td>Type</td><td colspan="2">Data gathering and enforcement method</td><td colspan="2">Data gathering/ screening</td><td colspan="2">Data gathering</td></tr>
<tr><td>Analytes</td><td colspan="2">Florasulam</td><td colspan="2">Florasulam</td><td colspan="2">Florasulam</td></tr>
</table>

Instrumentation	Capillary gas chromatography with mass selective detection (GC-MSD)	Immunoassay (ELISA)	LC-MS/MS
LOQ	0.01 ppm for grain; 0.057 ppm for forage; 0.0064 ppm (hay); 0.087 ppm (straw)–wheat, barley, oat	–	0.01 ppm
Standard	An external standard method was used as marker for retention time, response and calibration.	–	*N*-methyl florasulam internal standard
ILV	The recovery results (70 to 120%) obtained by an independent laboratory validated the enforcement method for the determination of florasulam in wheat, barley and oats.	–	–
Extraction/ clean-up	C$_{18}$ SPE column clean-up	C$_{18}$ SPE column clean-up	–
Multiresidue method	MRM cannot serve as an enforcement method since protocols are not suitable for the determination of florasulam.	–	–

Nature of the residue in wheat (immature plant and straw)		
Radiolabel	[UL-phenyl-^{14}C]florasulam	[9-tiazolopyrimidine-^{14}C]florasulam
Test Site	Tubs filled with sandy loam soil, outside.	
Treatment	Post emergent foliar application at growth stage BBCH30 or BBCH49	
Rate	50 g a.i./ha	
EP	EF-1343 (suspension concentrate)	
PHI	For plants treated at BBCH 30 stage: 0 (immature plant), 30 (immature plant), and 129 (straw) days. For plants treated at the BBCH 49 stage: 0 (immature plant), 30 (immature plant), and 65 (straw) days.	

Metabolites identified	Major metabolites (>10% TRRs)		Minor metabolites (<10% TRRs)	
Radiolabel	**[UL-phenyl-^{14}C]florasulam**	**[9-triazolopyrimidine-^{14}C]florasulam**	**[UL-phenyl-^{14}C]florasulam**	**[9-triazolopyrimidine-^{14}C]florasulam**
BBCH 30 (early application)				
Immature plant (0 and 30 days harvest)	florasulam, glucose conjugate of 4-OH-phenyl-florasulam	florasulam, glucose conjugate of 4-OH-phenyl-florasulam, 4-OH-phenyl-florasulam	4-OH-phenyl-florasulam	2-sulphonamide
Straw (129 day harvest)	–	–	glucose conjugate of 4-OH-phenyl-florasulam, 4-OH-phenyl-florasulam	2-sulphonamide, glucose conjugate of 4-OH-phenyl-florasulam,4-OH-phenyl-florasulam

STUDY	SPECIES OR STRAIN AND DOSES	NOAEL AND LOAEL (mg/kg bw/d)	TARGET ORGAN AND SIGNIFICANT EFFECTS AND COMMENTS

Recommended ADI: The most appropriate NOAEL of 5.0 mg/kg bw/d in the one-year dietary study in dogs is recommended as the basis for the ADI. Treatment-related findings at the LOAEL (next highest dose level) included lower body weight, body-weight gain and food consumption (♀), increased ALP activity (both sexes) and decreased serum albumin and protein levels (both sexes) at 50 mg/kg bw/d and increased severity of hypertrophy of the epithelial cells of the collecting ducts and slight vacuolization of the zona reticularis and zona fasciculata in the adrenal glands in both sexes at 100 and 50 mg/kg bw/d. A safety factor of 100 to account for intra- and inter-species variations was applied to this NOAEL to determine the ADI. No additional safety factor is required. The recommended ADI is 0.05 mg/kg bw/d.

MOE for other critical end point(s): calculated as NOAEL/ADI
Developmental toxicity: NOAEL = 250 mg/kg bw/d (rat). The MOE for developmental toxicity is 5000 compared with the ADI.
Two-generation reproduction study:
Reproductive toxicity: NOAEL = 500 mg/kg bw/d. The MOE is 10 000 compared with the ADI
Offspring toxicity: NOAEL = 100 mg/kg bw/d. The MOE is 2000 compared with the ADI

Table 6 Residues

Directions for use

Crop	Formulation type	Interval (days)	Rate (g a.i./ha)	Application/ season	Maximum rate (g a.i./ha)	PHI (days)
wheat (spring, durum), barley (spring), oat	EF-1343 Suspension concentrate (50 g/L)	postemergent 2-leaf crop up to and including the flag leaf extended stage	5	1	5	60

Physicochemical properties

Water solubility (g/L)	0.121; 0.084 (pH 5); 6.36 (pH 7); 94.2 (pH 9)
Solvent solubility (g/L)	123.0 (acetone); 72.1 (acetonitrile); 15.9 (ethyl acetate); 9.81 (methanol); 3.75 (dichloromethane); 0.227 (xylene); 0.184 (*n*-octanol); 0.000019 (*n*-heptane)
n-octanol–water partition coefficient (Log K_{ow})	1.00 (pH 4); -1.22 (pH 7); -2.06 (pH 10)
Dissociation constant (pK_a)	4.54
Vapour pressure (Pa)	1×10^{-5}
Melting point °C	193.5–230.5
UV-visible absorption spectrum	No absorbance at λ > 300 nm. 203.8–259.8 (acidic medium); 209.7–262.4 (basic medium); 204.1 (methanolic)

Analytical methodology

Parameters	**Plant matrices**		
Method ID	GRM 98.01	GRM 97.01	GRM 99.17
Type	Data gathering and enforcement method	Data gathering/ screening	Data gathering
Analytes	Florasulam	Florasulam	Florasulam

Instrumentation	Capillary gas chromatography with mass selective detection (GC-MSD)	Immunoassay (ELISA)	LC-MS/MS
LOQ	0.01 ppm for grain; 0.057 ppm for forage; 0.0064 ppm (hay); 0.087 ppm (straw)–wheat, barley, oat	–	0.01 ppm
Standard	An external standard method was used as marker for retention time, response and calibration.	–	*N*-methyl florasulam internal standard
ILV	The recovery results (70 to 120%) obtained by an independent laboratory validated the enforcement method for the determination of florasulam in wheat, barley and oats.	–	–
Extraction/ clean-up	C_{18} SPE column clean-up	C_{18} SPE column clean-up	–
Multiresidue method	MRM cannot serve as an enforcement method since protocols are not suitable for the determination of florasulam.	–	–

Nature of the residue in wheat (immature plant and straw)		
Radiolabel	[UL-phenyl-^{14}C]florasulam	[9-tiazolopyrimidine-^{14}C]florasulam
Test Site	Tubs filled with sandy loam soil, outside.	
Treatment	Post emergent foliar application at growth stage BBCH30 or BBCH49	
Rate	50 g a.i./ha	
EP	EF-1343 (suspension concentrate)	
PHI	For plants treated at BBCH 30 stage: 0 (immature plant), 30 (immature plant), and 129 (straw) days. For plants treated at the BBCH 49 stage: 0 (immature plant), 30 (immature plant), and 65 (straw) days.	

Metabolites identified	Major metabolites (>10% TRRs)		Minor metabolites (<10% TRRs)	
Radiolabel	[UL-phenyl-^{14}C]florasulam	[9-triazolopyrimidine-^{14}C]florasulam	[UL-phenyl-^{14}C]florasulam	[9-triazolopyrimidine-^{14}C]florasulam
BBCH 30 (early application)				
Immature plant (0 and 30 days harvest)	florasulam, glucose conjugate of 4-OH-phenyl-florasulam	florasulam, glucose conjugate of 4-OH-phenyl-florasulam, 4-OH-phenyl-florasulam	4-OH-phenyl-florasulam	2-sulphonamide
Straw (129 day harvest)	–	–	glucose conjugate of 4-OH-phenyl-florasulam, 4-OH-phenyl-florasulam	2-sulphonamide, glucose conjugate of 4-OH-phenyl-florasulam,4-OH-phenyl-florasulam

BBCH 49 (late application)				
Immature plant (0 and 30 days harvest)	florasulam, glucose conjugate of 4-OH-phenyl-florasulam	florasulam, glucose conjugate of 4-OH-phenyl-florasulam	4-OH-phenyl-florasulam	2-sulphonamide, 4-OH-phenyl-florasulam
Straw (65 day harvest)	florasulam, glucose conjugate of 4-OH-phenyl-florasulam, 4-OH-phenyl-florasulam	glucose conjugate of 4-OH-phenyl-florasulam	–	florasulam, 4-OH-phenyl-florasulam

Confined rotational crop study – spring wheat, sunflower, cabbage and carrots				
Radiolabels	[UL-phenyl-^{14}C]florasulam and [9-triazolopyrimidine-^{14}C]florasulam			
Test Site	Tubs of sandy loam soil			
Treatment	application to soil 30 days prior to planting			
Rate	7.5 g a.i./ha			
EP	EF-1343 (suspension concentrate)			
PHI	Cabbage 195 days, sunflower and spring wheat 168 days, and carrots 156 days.			
None of the TRRs in rotational crops were >0.01 ppm; therefore no further attempt to profile them was made. However, residues in soil were characterized.				
Metabolites identified in soil	Major metabolites (>10% TRRs)		Minor metabolites (<10% TRRs)	
Radiolabel	[UL-phenyl-^{14}C]florasulam	[9-triazolopyrimidine-^{14}C]florasulam	[UL-phenyl-^{14}C]florasulam	[9-triazolopyrimidine-^{14}C]florasulam
Spring wheat (0 day)	5-OH-florasulam, florasulam	5-OH-florasulam, florasulam	–	–
Spring wheat (30 day)	5-OH-florasulam, florasulam	5-OH-florasulam, florasulam	–	–
Sunflower (0 day)	florasulam	5-OH-florasulam, florasulam	5-OH-florasulam	–
Sunflower (30 day)	5-OH-florasulam, florasulam	5-OH-florasulam, florasulam	–	–
Cabbage (0 day)	5-OH-florasulam, florasulam	florasulam	–	–
Cabbage (30 day)	5-OH-florasulam, florasulam	5-OH-florasulam, florasulam	–	–
Carrot (0 day)	5-OH-florasulam, florasulam	5-OH-florasulam, florasulam	–	–
Carrot (30 day)	not profiled			

Nature of the residue in lactating goat			
Species	**Radiolabel**	**Dose level**	**Sacrifice**
Goat	UL-aniline [A] and 9-triazolopyrimidine [TP] (^{14}C)	11.2–11.3 ppm for 5 consecutive days	24 hrs after the last dose

Majority of the radioactivity was excreted in urine and feces accounting for a total of 99.8%. Residues in tissues, milk, and blood samples were less than 0.1% of the administered dose.

Metabolites identified	Major metabolites (>10% TRRs)		Minor metabolites (<10% TRRs)	
Radiolabel	UL-aniline [A]	9-triazolopyrimidine [TP]	UL-aniline [A]	9-triazolopyrimidine [TP]
Liver	florasulam	florasulam	5-OH-florasulam	5-OH-florasulam
Kidney	florasulam	florasulam	5-OH-florasulam	5-OH-florasulam
Fat	–	–	–	–
Muscle	–	–	–	–
Milk	florasulam	florasulam	5-OH-florasulam	5-OH-florasulam
Urine	florasulam	florasulam	5-OH-florasulam	5-OH-florasulam
Bile	–	–	–	–

Nature of the residue in laying hen

Species	Radiolabel	Dose level	Sacrifice
Laying Hen *(Gallus domesticus)*	UL-aniline [A] and 9-triazolopyrimidine [TP] (^{14}C)	10.5–10.9 ppm for 5 consecutive days	24 hrs after the last dose.

More than 90% of the administered dose was found in excreta. Residues in tissues and egg samples were low with only a small portion of the recovered radioactivity (< 0.02% of the TRRs, up to 0.004 ppm).

Metabolites identified	Major metabolites (>10% TRRs)		Minor metabolites (<10% TRRs)	
Radiolabel	UL-aniline [A]	9-triazolopyrimidine [TP]	UL-aniline [A]	9-triazolopyrimidine [TP]
muscle, fat, kidney, liver, egg white	florasulam	florasulam	–	–
egg yolk	florasulam	florasulam	–	–

Crop field trials – wheat, oat, barley and rye

A total of 44 supervised crop field trials were conducted encompassing regions 1, 5, 5A, 5B, 7, 7A, 8, and 14 on wheat, barley, rye, and oat during the 1997 and 2001 growing seasons.

Commodity	Rate kg a.i./ha	PHI (days)	Residue levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	SD
Analyte EF-1343									
Wheat									
Grain	9.77–9.88	50–60	14	0.005	0.005	–	–	–	–
Hay	9.81–9.88	7 15	5 4	0.028 0.023	0.071 0.058	0.067 0.058	0.062 0.052	0.056 0.046	0.0174 0.016
Forage	9.89–9.99	7 15	6 3	0.015 0.015	0.038 0.032	0.032 0.024	0.015 0.015	0.021 0.021	0.0095 0.0098
Straw	9.77–9.93	52–60	13	0.026	0.026	–	–	–	–

Oat									
Grain	9.88–10.2	47–54	9	0.005	0.005	–	–	–	–
Forage	9.90–10.39	7	6	0.015	0.015	–	–	–	–
Hay	9.88–10.2	7 15 30	4 1 1	0.015 0.015 0.022	0.054 0.015 0.022	0.049 – –	0.029 – –	0.032 – –	0.0198 – –
Straw	9.88–10.2	47–54	9	0.026	0.026	–	–	–	–
Barley									
Grain	9.87–9.92	56–58	7	0.005	0.005	–	–	–	–
Hay	9.87–9.92	7 15 30	2 1 2	0.015 0.015 0.015	0.015 0.015 0.015	– – –	– – –	– – –	– – –
Straw	9.87–9.92	56–58	7	0.026	0.026	–	–	–	–
Commodity	**Rate kg a.i./ha**	**PHI (days)**	**Residue levels (ppm)**						
			n	**Min.**	**Max.**	**HAFT**	**Median**	**Mean**	**SD**
Rye									
Grain	9.96	60	4	0.005	0.005	–	–	–	–
Forage	9.94	0 7 10 15	3 2 2 2	0.921 0.071 0.05 0.032	1.101 0.081 0.055 0.046	– – – –	1.068 0.076 0.0525 0.039	1.03 0.076 0.0525 0.039	0.0958 0.007 0.003 0.0098
Straw	9.96	60	3	0.026	0.026	–	–	–	–
GRM 99.17									
Oat Grain	9.96	60	2	0.003	0.003	–	–	–	–
Barley Grain	9.8–10.2	54–58	4	0.003	0.003	–	–	–	–

Freezer storage stability

The data presented indicated that residues of florasulam were stable at -20°C for a duration of 498, 524, 410, and 313 days in the spiked wheat dried plants, forage, grain, and straw. The freezer storage stability data for wheat can be extended to barley and oat matrices. Significant degradation was observed in immature green plants (38% over 498 days) and in hay (31% over 459 days). A correction factor on immature green plant and hay residue values in the crop field trial was necessary due to in storage dissipation.

Maximum residue limits

Wheat, barley, oat	0.01 ppm

Processing studies

It is unlikely that residues of florasulam in processed food items will concentrate when treated according to the proposed Canadian use pattern.

Livestock feeding

Livestock feeding studies are not required in support of this petition based on the livestock metabolism studies. No finite residues of florasulam are expected in the livestock tissues, milk, and eggs.

Table 7 Overview of metabolism studies and risk assessment

Plant studies			
ROC for enforcement and risk assessment		Florasulam	
Rotational crops		Florasulam	
Metabolic profile in diverse crops		Only wheat was evaluated	
Animal studies – lactating goat, laying hen			
ROC for enforcement and risk assessment		Florasulam	
Metabolic profile in animals		Similar	
Fat-soluble residue		No	
DIETARY RISK FROM FOOD AND WATER			
Chronic non-cancer dietary risk **ADI = 0.05 mg/kg bw/day**	**POPULATION**	**ESTIMATED RISK (% of ADI)**	
		Food (MRLs)	**Food + water**
	All infants < 1 yr old	0	10
	Children 1 to 2 yrs	0.1	10.1
	Children 3 to 5 yrs	0.1	10.1
	Children 6 to 12 yrs	0.1	10.1
	Youth 13 to 19 yrs	0	10
	Adults 20 to 49 yrs	0	10
	Adults 50+ yrs	0	10
	Females 13 to 49 yrs	0	10
	Total Population	0	10

Table 8 Maximum EEC in vegetation and insects after a direct overspray

Matrix	EEC (mg a.i./kg fw)[a]	Fresh to dry weight ratios	EEC (mg a.i./kg dw)
Short-range grass	1.07	3.3[b]	3.5311
Leaves and leafy crops	0.56	11[b]	6.16
Long grass	0.49	4.4[b]	2.156
Forage crops	0.26	5.4[b]	1.404
Small insects	0.26	3.8[c]	0.988
Pods with seeds	0.0535	3.9[c]	0.2087
Large insects	0.0445	3.8[c]	0.1691
Grain and seeds	0.0445	3.8[c]	0.1691
Fruit	0.031	7.6[c]	0.2356

[a] Based on correlations reported in Hoerger and Kenaga (1972) and Kenaga (1973)

[b] Fresh to dry weight ratios from Harris (1975)

[c] Fresh to dry weight ratios from Spector (1956)

Table 9 Physical and chemical properties of florasulam relevant to the environment

Property	Value	Comments
Water solubility (g/L)	pH Solubility 5 0.084 7 6.36 9 94.2	Soluble at pH 5 and very soluble at pH 7 and 9
Vapour pressure (Pa)	1×10^{-5} at 25°C	Relatively non-volatile
K	2.97×10^{-5} Pa m^3 mol^{-1}	Non-volatile from a water or moist soil surface
log K_{ow}	pH log K_{ow} 4 or 5 1.00 7 −1.85 9 or 10 −2.06	Bioconcentration is unlikely
pK_a	4.54	Neutral molecule will predominate at pH > 4.54. Adsorption will decrease as pH increases
UV–visible absorption	Form λmax Acidic 259.8 203.8 Basic 262.4 209.7 Methanolic 204.1 No absorbance maxima above 300 nm	Low potential for phototransformation

Table 10 Physical and chemical properties of 5-hydroxy-XDE-570 relevant to the environment

Property	Value	Comments
Water solubility at 20°C (g/L)	pH / Solubility 5 / 0.633 7 / > 450.0 9 / > 800.0	Very soluble at all environmentally relevant pH
Vapour pressure (Pa)	2.7×10^{-6} at 25°C	Relatively non-volatile
K	2.63×10^{-6} Pa m^3 mol^{-1}	Nonvolatile from a water or moist soil surface
log K_{ow}	pH / log K_{ow} 5 / 0.32 7 / −1.85 9 / −2.32	Bioconcentration is unlikely.
pK_a	4.53 (pH = 3.0–5.5) 7.22 (pH = 6.0–8.5)	Neutral molecule will predominate at pH > 4.53 and anionic form will predominate at pH > 7.22.

Table 11 Fate and behaviour in the terrestrial environment

Study	Test substance[a]	Value or result	Comments
Abiotic transformation			
Hydrolysis	PH- and TP-labelled ^{14}C-florasulam	At pH 5 and 7, no hydrolysis at 25°C for 30 d At pH 9, $t_{½}$ = 98–100 at 25°C and 219–226 d at 20°C	Not an important route of transformation
Phototransformation on soil	AN- and TP-labelled ^{14}C-florasulam	$t_{½}$ = 62 d	Not an important route for transformation
Biotransformation			
Biotransformation in aerobic soil	TP- and PH-labelled ^{14}C-florasulam	**Study 1** $t_{½}$ of florasulam = 0.7–4.5 d $t_{½}$ of 5-hydroxy-XDE-570 = 10–31 d	Florasulam is non-persistent. 5-hydroxy-XDE-570 is non-persistent to moderately persistent. Important route of transformation
	TP-labelled ^{14}C-florasulam	**Study 2** Half-life of florasulam = 3.9–8.3 d Half-life of 5-hydroxy-XDE-570 = 34–56 d	Florasulam is non-persistent. 5-hydroxy-XDE-570 is moderately persistent.

Table 8 Maximum EEC in vegetation and insects after a direct overspray

Matrix	EEC (mg a.i./kg fw)[a]	Fresh to dry weight ratios	EEC (mg a.i./kg dw)
Short-range grass	1.07	3.3[b]	3.5311
Leaves and leafy crops	0.56	11[b]	6.16
Long grass	0.49	4.4[b]	2.156
Forage crops	0.26	5.4[b]	1.404
Small insects	0.26	3.8[c]	0.988
Pods with seeds	0.0535	3.9[c]	0.2087
Large insects	0.0445	3.8[c]	0.1691
Grain and seeds	0.0445	3.8[c]	0.1691
Fruit	0.031	7.6[c]	0.2356

[a] Based on correlations reported in Hoerger and Kenaga (1972) and Kenaga (1973)
[b] Fresh to dry weight ratios from Harris (1975)
[c] Fresh to dry weight ratios from Spector (1956)

Table 9 Physical and chemical properties of florasulam relevant to the environment

Property	Value	Comments
Water solubility (g/L)	pH Solubility 5 0.084 7 6.36 9 94.2	Soluble at pH 5 and very soluble at pH 7 and 9
Vapour pressure (Pa)	$1 \times 10^{[illegible]}$ at 25°C	Relatively non-volatile
K	$2.97 \times 10^{[illegible]}$ Pa m^3 mol^{-1}	Non-volatile from a water or moist soil surface
log K_{ow}	pH log K_{ow} 4 or 5 1.00 7 -1.85 9 or 10 -2.06	Bioconcentration is unlikely
pK_a	4.54	Neutral molecule will predominate at pH > 4.54. Adsorption will decrease as pH increases
UV-visible absorption	Form λmax Acidic 259.8 203.8 Basic 262.4 209.7 Methanolic 204.1 No absorbance maxima above 300 nm	Low potential for phototransformation

Table 10 Physical and chemical properties of 5-hydroxy-XDE-570 relevant to the environment

Property	Value	Comments
Water solubility at 20°C (g/L)	pH Solubility 5 0.633 7 >450.0 9 >800.0	Very soluble at all environmentally relevant pH
Vapour pressure (Pa)	2.7 × 10[illegible] at 25°C	Relatively non-volatile
K	2.63 × 10[illegible] Pa m^3 mol^{-1}	Nonvolatile from a water or moist soil surface
$\log K_{ow}$	pH $\log K_{ow}$ 5 0.32 7 −1.85 9 −2.32	Bioconcentration is unlikely.
pK_a	4.53 (pH = 3.0–5.5) 7.22 (pH = 6.0–8.5)	Neutral molecule will predominate at pH > 4.53 and anionic form will predominate at pH > 7.22.

Table 11 Fate and behaviour in the terrestrial environment

Study	Test substance[a]	Value or result	Comments
Abiotic transformation			
Hydrolysis	PH- and TP-labelled ^{14}C-florasulam	At pH 5 and 7, no hydrolysis at 25°C for 30 d At pH 9, $t_{1/2}$ = 98–100 at 25°C and 219–226 d at 20°C	Not an important route of transformation
Phototransformation on soil	AN- and TP-labelled ^{14}C-florasulam	$t_{1/2}$ = 62 d	Not an important route for transformation
Biotransformation			
Biotransformation in aerobic soil	TP- and PH-labelled ^{14}C-florasulam	**Study 1** $t_{1/2}$ of florasulam = 0.7–4.5 d $t_{1/2}$ of 5-hydroxy-XDE-570 = 10–31 d	Florasulam is non-persistent. 5-hydroxy-XDE-570 is non-persistent to moderately persistent. Important route of transformation
	TP-labelled ^{14}C-florasulam	**Study 2** Half-life of florasulam = 3.9–8.3 d Half-life of 5-hydroxy-XDE-570 = 34–56 d	Florasulam is non-persistent. 5-hydroxy-XDE-570 is moderately persistent.

Study	Test substance[a]	Value or result	Comments
Mobility			
Adsorption and desorption in soil	PH-labelled ^{14}C-florasulam and ^{14}C-5-hydroxy-XDE-570	Adsorption K_d = 0.08–0.94 for florasulam and 0.16–0.72 for 5-hydroxy-XDE-570 Desorption K_d = 0.49–1.45 for florasulam and 0.30–0.76 for 5-hydroxy-XDE-570	High to very high mobility for florasulam and 5-hydroxy-XDE-570
Soil leaching	TP-labelled ^{14}C-florasulam	67.7–92.1% leached through the soil columns	Very high leaching potential
Field studies			
Field dissipation	EF-1343	DT_{50} for florasulam = 2–10 d DT_{90} = 16–34 d Florasulam and 5-hydroxy-XDE-570 are leachable when there is excessive rainfall or irrigation.	Florasulam is non-persistent. Carry-over is not expected. 5-hydroxy-XDE-570 can persist and carry over.

[a] TP-labelled = triazolopyrimidine-labelled; PH-labelled = phenyl-labelled; AN-labelled = aniline-labelled

Table 12 Summary of transformation products formed in terrestrial fate studies

Study	Major transformation product (maximum concentration as % of applied)	Minor transformation products (maximum concentration as % of applied)
Hydrolysis	5-hydroxy-XDE-570, *N*-(2,6-difluorphenyl)-8-fluoro-5-hydroxy(1,2,4)triazolo(1,5*c*)pyrimidine-2-sulphonamide (14% at 20°C and 32% at 25°C both at day 90, the end of test) A second hydrolysis product that might be formed by addition of water to triazolopyrimidine ring of parent compound (13% at 20°C and 17% at 25°C both at day 90, the end of test)	No minor transformation products detected
Phototransformation on soil	Transformation products were the same in exposed and dark control samples, indicating that they were formed by biotransformation. 5-hydroxy-XDE-570 Another transformation product, tentatively identified as amino sulfinyltriazolopyrimidine-florasulam [8-fluoro-5-methoxy(1,2,4)triazolo(1,5*c*)-pyrimidine-2-sulphonamide]	At least 5 minor transformation products detected: vinyl fluoridetriazolo-florasulam florasulam triazolo carboxylic acid triazolo-florasulam two unidentified minor transformation products

Study	Major transformation product (maximum concentration as % of applied)	Minor transformation products (maximum concentration as % of applied)
Aerobic biotransformation in soil	Study 1: 5-hydroxy-XDE-570 (72% at day 3) *N*-(2,6-difluorophenyl)-5-aminosulphonyl-1*H*-1,2,4-triazole-3-carboxylic acid (DFP-ASTCA) (18% at day 59) 5-(aminosulphonyl)-1*H*-1,2,4-triazole-3-carboxylic acid (ASTCA) (40% at day 59) 1*H*-1,2,4-triazole-3-sulphonamide (TSA) (16% at day 100)	Four minor transformation products each accounted for <5% DFP-TSA [*N*-(2,6-difluorophenyl)-1*H*-1,2,4-triazole-3-sulphonamide] (<4%) Three unidentified minor transformation products
	Study 2: 5-hydroxy-XDE-570 (50% at day 14) triazolosulfonic carboxylic acid (STCA) triazolosulfonic acid (STA) aminosulfonyltriazolo carboxylic acid (ASTCA) aminosulfonyltriazole (TSA) difluorophenyl aminosulfonyltriazolo carboxylic acid (DFP-ASTCA) difluorophenyl aminosulfonyltriazole (DFP-AST) and three other unidentifiable compounds (as a group, reached 67% at test termination)	Four unidentified minor transformation products (each <6%)
Field dissipation	5-hydroxy-XDE-570 (59% at day 28)	DFP-ASTCA (<3%)

Table 13 Fate and behaviour in the aquatic environment

Study	Test material	Value or results	Comments
Abiotic transformation			
Hydrolysis		See Appendix I, Table 11	
Phototransformation in water	AN- and TP-labelled ^{14}C-florasulam	$t_{1/2}$ = 88– 223 d	Not an important route of transformation
Biotransformation			
Biotransformation in aerobic water and sediment	TP- and AN-labelled ^{14}C-florasulam	$t_{1/2}$ of florasulam = 3 d (25°C) $t_{1/2}$ of 5-hydroxy-XDE-570 = 169 d (25°C)	Florasulam is non-persistent. 5-hydroxy-XDE-570 is persistent.
Biotransformation in aerobic water and anaerobic sediment	TP- and PH-labelled ^{14}C-florasulam	$t_{1/2}$ of florasulam = 8.7–18 d (20°C) Half-life of 5-hydroxy-XDE-570 = 69–244 d (20°C)	Florasulam is non-persistent to slightly persistent. 5-hydroxy-XDE-570 is moderately persistent to persistent.

Study	Test substance[a]	Value or result	Comments
Mobility			
Adsorption and desorption in soil	PH-labelled ^{14}C-florasulam and ^{14}C-5-hydroxy-XDE-570	Adsorption K_d = 0.08–0.94 for florasulam and 0.16–0.72 for 5-hydroxy-XDE-570 Desorption K_d = 0.49–1.45 for florasulam and 0.30–0.76 for 5-hydroxy-XDE-570	High to very high mobility for florasulam and 5-hydroxy-XDE-570
Soil leaching	TP-labelled ^{14}C-florasulam	67.7–92.1% leached through the soil columns	Very high leaching potential
Field studies			
Field dissipation	EF-1343	DT_{50} for florasulam = 2–10 d DT_{90} = 16–34 d Florasulam and 5-hydroxy-XDE-570 are leachable when there is excessive rainfall or irrigation.	Florasulam is non-persistent. Carry-over is not expected. 5-hydroxy-XDE-570 can persist and carry over.

[a] TP-labelled = triazolopyrimidine-labelled; PH-labelled = phenyl-labelled; AN-labelled = aniline-labelled

Table 12 Summary of transformation products formed in terrestrial fate studies

Study	Major transformation product (maximum concentration as % of applied)	Minor transformation products (maximum concentration as % of applied)
Hydrolysis	5-hydroxy-XDE-570, *N*-(2,6-difluorphenyl)-8-fluoro-5-hydroxy(1,2,4)triazolo(1,5*c*)pyrimidine-2-sulphonamide (14% at 20°C and 32% at 25°C both at day 90, the end of test) A second hydrolysis product that might be formed by addition of water to triazolopyrimidine ring of parent compound (13% at 20°C and 17% at 25°C both at day 90, the end of test)	No minor transformation products detected
Phototransformation on soil	Transformation products were the same in exposed and dark control samples, indicating that they were formed by biotransformation. 5-hydroxy-XDE-570 Another transformation product, tentatively identified as amino sulfinyltriazolopyrimidine-florasulam [8-fluoro-5-methoxy(1,2,4)triazolo(1,5*c*)-pyrimidine-2-sulphonamide]	At least 5 minor transformation products detected: vinyl fluoridetriazolo-florasulam florasulam triazolo carboxylic acid triazolo-florasulam two unidentified minor transformation products

Study	Major transformation product (maximum concentration as % of applied)	Minor transformation products (maximum concentration as % of applied)
Aerobic biotransformation in soil	Study 1: 5-hydroxy-XDE-570 (72% at day 3) *N*-(2,6-difluorophenyl)-5-aminosulphonyl-1*H*-1,2,4-triazole-3-carboxylic acid (DFP-ASTCA) (18% at day 59) 5-(aminosulphonyl)-1*H*-1,2,4-triazole-3-carboxylic acid (ASTCA) (40% at day 59) 1*H*-1,2,4-triazole-3-sulphonamide (TSA) (16% at day 100)	Four minor transformation products each accounted for <5% DFP-TSA [*N*-(2,6-difluorophenyl)-1*H*-1,2,4-triazole-3-sulphonamide] (<4%) Three unidentified minor transformation products
	Study 2: 5-hydroxy-XDE-570 (50% at day 14) triazolosulfonic carboxylic acid (STCA) triazolosulfonic acid (STA) aminosulfonyltriazolo carboxylic acid (ASTCA) aminosulfonyltriazole (TSA) difluorophenyl aminosulfonyltriazolo carboxylic acid (DFP-ASTCA) difluorophenyl aminosulfonyltriazole (DFP-AST) and three other unidentifiable compounds (as a group, reached 67% at test termination)	Four unidentified minor transformation products (each <6%)
Field dissipation	5-hydroxy-XDE-570 (59% at day 28)	DFP-ASTCA (<3%)

Table 13 Fate and behaviour in the aquatic environment

Study	Test material	Value or results	Comments
Abiotic transformation			
Hydrolysis		See Appendix I, Table 11	
Phototransformation in water	AN- and TP-labelled ^{14}C-florasulam	$t_{1/2}$ = 88–223 d	Not an important route of transformation
Biotransformation			
Biotransformation in aerobic water and sediment	TP- and AN-labelled ^{14}C-florasulam	$t_{1/2}$ of florasulam = 3 d (25°C) $t_{1/2}$ of 5-hydroxy-XDE-570 = 169 d (25°C)	Florasulam is non-persistent. 5-hydroxy-XDE-570 is persistent.
Biotransformation in aerobic water and anaerobic sediment	TP- and PH-labelled ^{14}C-florasulam	$t_{1/2}$ of florasulam = 8.7–18 d (20°C) Half-life of 5-hydroxy-XDE-570 = 69–244 d (20°C)	Florasulam is non-persistent to slightly persistent. 5-hydroxy-XDE-570 is moderately persistent to persistent.

Study	Test material	Value or results	Comments
Biotransformation in anaerobic water and sediment	TP- and AN-labelled ^{14}C-florasulam	In a water and soil system, $t_{1/2}$ of florasulam = 13 d. In a water and natural pond sediment system, $t_{1/2} < 2$ d. For 5-hydroxy-XDE-570, 0.3% of applied at day 0, maximum of 87% at day 97 and 78% at day 368	Florasulam is non-persistent. 5-hydroxy-XDE-570 is persistent
Partitioning			
Adsorption and desorption in sediment		In the above water and sediment studies, adsorption of florasulam and 5-hydroxy-XDE-570 to sediment was low.	Low partitioning into sediment

Table 14 Summary of transformation products formed in aquatic fate studies

Study	Major transformation product (maximum concentration as % of applied)	Minor transformation products (maximum concentration as % of applied)
Hydrolysis	5-hydroxy-XDE-570, *N*-(2,6-difluorphenyl)-8-fluoro-5-hydroxy(1,2,4)triazolo (1,5*c*)pyrimidine-2-sulphonamide (14% at 20°C and 32% at 25°C both at day 90, the end of test) A second hydrolysis product that might be formed by addition of water to triazolopyrimidine ring of parent compound (13% at 20°C and 17% at 25°C both at day 90, the end of test)	No minor transformation products detected
Phototransformation in water	TPSA of florasulam (17% at test termination)	Several unidentified minor transformation products (<6% as a group at test termination)
Biotransformation in aerobic water and sediment	5-hydroxy-XDE-570 (80% at day 10) DFP-ASTCA (26% at 91) A compound tentatively identified as STCA (31% at day 91)	A compound unidentified minor transformation product (<9%)
Biotransformation in aerobic water and anaerobic sediment	5-hydroxy-XDE-570 (99% at day 60) DFP-ASTCA (39% at test termination) An unstable intermediate transformation product occurs between the 5-hydroxy-XDE-570 and DFP-ASTCA and is readily broken down to DFP-ASTCA (14.2% at day 100).	A compound unidentified minor transformation product (<6%)
Biotransformation in anaerobic water and sediment	5-hydroxy-XDE-570 (87% at day 97)	One tentatively identified as *N*-(2,6-difluorophenyl)-5-amino-sulphonyl-1–methyl-1,2,4-triazole-3-carboxylic acid (7.8% at test termination)

Table 15 Effects on terrestrial organisms

Organism	Exposure	Test substance	End point value	Degree of toxicity
Invertebrates				
Earthworm	Acute	Florasulam	14-d $LC_{50} > 1300$ mg a.i./kg soil 14-d NOEC = 1300 mg a.i./kg soil	N/A
		5-hydroxy-XDE-570	14-d $LC_{50} > 1120$ mg a.i./kg soil 14-d NOEC = 1120 mg a.i./kg soil	N/A
		DFP-ASTCA, ASTCA and TSA	14-d $LC_{50} > 100$ µg a.i./kg soil 14-d NOEC = 10 µg a.i./kg soil	N/A
		STA and STCA	14-d $LC_{50} > 100$ µg a.i./kg soil 14-d NOEC = 100 µg a.i./kg soil	N/A
Bee	Oral	Florasulam	48-h $LC_{50} > 100$ µg a.i./bee	Relatively non-toxic
	Contact	Florasulam	48-h $LD_{50} > 100$ µg a.i./bee, 48-h NOEC = 100 µg a.i./bee	Relatively non-toxic
Birds				
Japanese quail	Acute oral	Florasulam	14-d $LD_{50} = 1047$ mg a.i./kg bw 14-d NOEL = 175 mg a.i./kg bw	Slightly toxic
	Dietary	Florasulam	8-d $LC_{50} > 5000$ mg a.i./kg diet 8-d NOEC = 5000 mg a.i./kg diet	Practically non-toxic
Bobwhite quail	Reproduction	Florasulam	NOEC = 1500 mg a.i./kg diet $LC_{50} > 1500$ mg a.i./kg diet	N/A
Mallard duck	Dietary	Florasulam	8-d $LD_{50} > 5000$ mg a.i./kg diet 8-d NOEC = 5000 mg a.i./kg diet	Practically non-toxic
	Reproduction	Florasulam	NOEC = 1500 mg a.i./kg diet $LC_{50} > 1500$ mg a.i./kg diet	N/A
Mammals				
Rat	Acute oral	Florasulam	$LD_{50} > 6000$ mg a.i./kg bw	Practically non-toxic
	90-d Dietary	Florasulam	NOAEL = 100 mg a.i./kg bw/d	N/A
	two-generation Reproduction	Florasulam	Parental and offspring NOAEL = 100 mg a.i./kg bw/d Reproductive NOAEL = 500 mg a.i./kg bw/d	N/A
	Acute inhalation	Florasulam	$LC_{50} > 5$ mg/L	Low toxicity
Mouse	Acute oral	Florasulam	$LD_{50} > 5000$ mg a.i./kg bw	Practically non-toxic
	90-d dietary	Florasulam	NOAEL = 100 mg a.i./kg bw/d	N/A

Study	Test material	Value or results	Comments
Biotransformation in anaerobic water and sediment	TP- and AN-labelled ^{14}C-florasulam	In a water and soil system, $t_{1/2}$ of florasulam = 13 d. In a water and natural pond sediment system, $t_{1/2}$ < 2 d. For 5-hydroxy-XDE-570, 0.3% of applied at day 0, maximum of 87% at day 97 and 78% at day 368	Florasulam is non-persistent. 5-hydroxy-XDE-570 is persistent
Partitioning			
Adsorption and desorption in sediment		In the above water and sediment studies, adsorption of florasulam and 5-hydroxy-XDE-570 to sediment was low.	Low partitioning into sediment

Table 14 Summary of transformation products formed in aquatic fate studies

Study	Major transformation product (maximum concentration as % of applied)	Minor transformation products (maximum concentration as % of applied)
Hydrolysis	5-hydroxy-XDE-570, *N*-(2,6-difluorphenyl)-8-fluoro-5-hydroxy(1,2,4)triazolo (1,5*c*)pyrimidine-2-sulphonamide (14% at 20°C and 32% at 25°C both at day 90, the end of test) A second hydrolysis product that might be formed by addition of water to triazolopyrimidine ring of parent compound (13% at 20°C and 17% at 25°C both at day 90, the end of test)	No minor transformation products detected
Phototransformation in water	TPSA of florasulam (17% at test termination)	Several unidentified minor transformation products (<6% as a group at test termination)
Biotransformation in aerobic water and sediment	5-hydroxy-XDE-570 (80% at day 10) DFP-ASTCA (26% at 91) A compound tentatively identified as STCA (31% at day 91)	A compound unidentified minor transformation product (<9%)
Biotransformation in aerobic water and anaerobic sediment	5-hydroxy-XDE-570 (99% at day 60) DFP-ASTCA (39% at test termination) An unstable intermediate transformation product occurs between the 5-hydroxy-XDE-570 and DFP-ASTCA and is readily broken down to DFP-ASTCA (14.2% at day 100).	A compound unidentified minor transformation product (<6%)
Biotransformation in anaerobic water and sediment	5-hydroxy-XDE-570 (87% at day 97)	One tentatively identified as *N*-(2,6-difluorophenyl)-5-amino-sulphonyl-1–methyl-1,2,4-triazole-3-carboxylic acid (7.8% at test termination)

Table 15 Effects on terrestrial organisms

Organism	Exposure	Test substance	End point value	Degree of toxicity^a
Invertebrates				
Earthworm	Acute	Florasulam	14-d LC_{50} > 1300 mg a.i./kg soil 14-d NOEC = 1300 mg a.i./kg soil	N/A
		5-hydroxy-XDE-570	14-d LC_{50} > 1120 mg a.i./kg soil 14-d NOEC = 1120 mg a.i./kg soil	N/A
		DFP-ASTCA, ASTCA and TSA	14-d LC_{50} > 100 µg a.i./kg soil 14-d NOEC = 10 µg a.i./kg soil	N/A
		STA and STCA	14-d LC_{50} > 100 µg a.i./kg soil 14-d NOEC = 100 µg a.i./kg soil	N/A
Bee	Oral	Florasulam	48-h LC_{50} > 100 µg a.i./bee	Relatively non-toxic
	Contact	Florasulam	48-h LD_{50} > 100 µg a.i./bee, 48-h NOEC = 100 µg a.i./bee	Relatively non-toxic
Birds				
Japanese quail	Acute oral	Florasulam	14-d LD_{50} = 1047 mg a.i./kg bw 14-d NOEL = 175 mg a.i./kg bw	Slightly toxic
	Dietary	Florasulam	8-d LC_{50} > 5000 mg a.i./kg diet 8-d NOEC = 5000 mg a.i./kg diet	Practically non-toxic
Bobwhite quail	Reproduction	Florasulam	NOEC = 1500 mg a.i./kg diet LC_{50} > 1500 mg a.i./kg diet	N/A
Mallard duck	Dietary	Florasulam	8-d LD_{50} > 5000 mg a.i./kg diet 8-d NOEC = 5000 mg a.i./kg diet	Practically non-toxic
	Reproduction	Florasulam	NOEC = 1500 mg a.i./kg diet LC_{50} > 1500 mg a.i./kg diet	N/A
Mammals				
Rat	Acute oral	Florasulam	LD_{50} > 6000 mg a.i./kg bw	Practically non-toxic
	90-d Dietary	Florasulam	NOAEL = 100 mg a.i./kg bw/d	N/A
	two-generation Reproduction	Florasulam	Parental and offspring NOAEL = 100 mg a.i./kg bw/d Reproductive NOAEL = 500 mg a.i./kg bw/d	N/A
	Acute inhalation	Florasulam	LC_{50} > 5 mg/L	Low toxicity
Mouse	Acute oral	Florasulam	LD_{50} > 5000 mg a.i./kg bw	Practically non-toxic
	90-d dietary	Florasulam	NOAEL = 100 mg a.i./kg bw/d	N/A

Organism	Exposure	Test substance	End point value	Degree of toxicity[a]
Rabbit	Acute dermal	Florasulam	$LD_{50} > 200$ mg a.i./kg bw	Low toxicity
Vascular plants				
Vascular plant	Seedling emergence	EF-1343	$EC_{25} = 4.3$ g a.i./ha visual rating on radish. For all other species, the EC_{25} and EC_{50} values were all >10 g a.i./ha.	N/A
	Vegetative vigour	EF-1343	Least activity on the monocot species. EC_{25} values for tomato, carrot, radish, sunflower, cucumber and soybean were 0.02, 0.09, 0.07, 0.04, 0.35 and 0.2 g a.i./ha, respectively.	N/A

[a] Atkins et al. (1981) for bees and USEPA classification for others, where applicable

Table 16 Effects on aquatic organisms

Organism	Exposure	Test substance	End point value	Degree of toxicity[a]
Freshwater species				
Daphnia magna	Acute	Florasulam	48-h LC_{50} or $EC_{50} > 292$ mg a.i./L 48-h NOEC = 174 mg a.i./L	Practically non-toxic
		EF-1343	48-h $EC_{50} > 100$ mg EF-1343/L (5.5 mg a.i./L) 48-h NOEC = 100 mg EF-1343/L (5.5 mg a.i./L)	Practically non-toxic
		5-hydroxy-XDE-570	48-h LC_{50} or $EC_{50} > 96.7$ mg a.i./L 48-h NOEC = 96.7 mg a.i./L	Practically non-toxic
	Chronic	Florasulam	21-d $LC_{50} = 169.2$ mg a.i./L 21-d NOEC = 38.9 mg a.i./L	N/A
Rainbow trout	Acute	Florasulam	96-h $LC_{50} > 100$ mg a.i./L 96-h NOEC = 100 mg a.i./L	Practically non-toxic
		EF-1343	96-h $LC_{50} > 100$ mg EF-1343/L (5.7 mg a.i./L) 96-h NOEC = 100 mg EF-1343/L (5.7 mg a.i./L)	Practically non-toxic
		5-hydroxy-XDE-570	96-h $LC_{50} > 100$ mg a.i./L 96-h NOEC = 100 mg a.i./L	Practically non-toxic
	Chronic	Florasulam	28-d $LC_{50} > 119$ mg a.i./L 28-d NOEC = 119 mg a.i./L	Practically non-toxic
Bluegill sunfish	Acute	Florasulam	96-h $LC_{50} > 100$ mg a.i./L 96-h NOEC = 100 mg a.i./L	Practically non-toxic
Freshwater alga	Acute	Florasulam	diatom cell count 5-d $EC_{25} = 0.18$ mg a.i./L 5-d $EC_{50} = 0.97$ mg a.i./L 5-d NOEC = 0.049 mg a.i./L	N/A

Organism	Exposure	Test substance	End point value	Degree of toxicity[a]
		EF-1343	green algae biomass 72-h EC_{50} = 3.45 μg a.i./L 72-h NOEC = 1.75 μg a.i./L	N/A
		5-hydroxy-XDE-570	green algae cell count 96-h EC_{25} = 11.59 mg a.i./L 96-h EC_{50} = 25.57 mg a.i./L 96-h NOEC = 6.64 mg a.i./L	N/A
Vascular plant	Dissolved	Florasulam	duckweed frond number 14-d EC_{25} = 0.57 μg a.i./L 14-d EC_{50} = 1.18 μg a.i./L 14-d NOEC = 0.62 μg a.i./L	N/A
Marine species				
Crustacean	Acute	Florasulam	grass shrimp 96-h LC_{50} > 130 mg a.i./L 96-h NOEC = 130 mg a.i./L	Practically non-toxic
Mollusk	Acute	Florasulam	oyster shell deposition 96-h LC_{50} > 125 mg a.i./L 96-h NOEC = 125 mg a.i./L	Practically non-toxic
Fish	Acute	Florasulam	silverside 96-h LC_{50} > 122 mg a.i./L 96-h NOEC = 122 mg a.i./L	Practically non-toxic
Marine alga	Acute	Florasulam	marine diatom 5-d EC_{25} = 32.4 mg a.i./L 5-d EC_{50} = 47.6 mg a.i./L 5-d NOEC = 22.8 mg a.i./L	N/A

[a] USEPA classification, where applicable

Table 17 Risk to terrestrial organisms

Organism	Exposure	End point value	EEC	MOS	Risk
Invertebrates					
Earthworm	Acute	14-d NOEC = 1300 mg a.i./kg soil	0.0022 mg a.i./kg soil	5.9×10^5	No risk
Bee	Contact	NOEC 112 kg a.i./ha	5 g a.i./ha	2.2×10^4	No risk
Birds					
Japanese quail	Acute oral	14-d NOEC = 175 mg a.i./kg bw	0.6 mg a.i./kg dw diet	1.2×10^3 d	No risk
	Dietary	8-d NOEC = 5000 mg a.i./kg diet	0.6 mg a.i./kg dw diet	8.3×10^3	No risk
Bobwhite quail	Reproduction	NOEC = 1500 mg a.i./kg diet	0.6 mg a.i./kg dw diet	2.5×10^3	No risk
Mammals					
Mouse	Acute	LD_{50} > 5000 mg a.i./kg bw	2.51 mg a.i./kg dw diet	> 9.2×10^3 d	No risk

Organism	Exposure	Test substance	End point value	Degree of toxicity[a]
Rabbit	Acute dermal	Florasulam	LD_{50} > 200 mg a.i./kg bw	Low toxicity
Vascular plants				
Vascular plant	Seedling emergence	EF-1343	EC_{25} = 4.3 g a.i./ha visual rating on radish. For all other species, the EC_{25} and EC_{50} values were all >10 g a.i./ha.	N/A
	Vegetative vigour	EF-1343	Least activity on the monocot species. EC_{25} values for tomato, carrot, radish, sunflower, cucumber and soybean were 0.02, 0.09, 0.07, 0.04, 0.35 and 0.2 g a.i./ha, respectively.	N/A

[a] Atkins et al. (1981) for bees and USEPA classification for others, where applicable

Table 16 Effects on aquatic organisms

Organism	Exposure	Test substance	End point value	Degree of toxicity[a]
Freshwater species				
Daphnia magna	Acute	Florasulam	48-h LC_{50} or EC_{50} > 292 mg a.i./L 48-h NOEC = 174 mg a.i./L	Practically non-toxic
		EF-1343	48-h EC_{50} > 100 mg EF-1343/L (5.5 mg a.i./L) 48-h NOEC = 100 mg EF-1343/L (5.5 mg a.i./L)	Practically non-toxic
		5-hydroxy-XDE-570	48-h LC_{50} or EC_{50} > 96.7 mg a.i./L 48-h NOEC = 96.7 mg a.i./L	Practically non-toxic
	Chronic	Florasulam	21-d LC_{50} = 169.2 mg a.i./L 21-d NOEC = 38.9 mg a.i./L	N/A
Rainbow trout	Acute	Florasulam	96-h LC_{50} > 100 mg a.i./L 96-h NOEC = 100 mg a.i./L	Practically non-toxic
		EF-1343	96-h LC_{50} > 100 mg EF-1343/L (5.7 mg a.i./L) 96-h NOEC = 100 mg EF-1343/L (5.7 mg a.i./L)	Practically non-toxic
		5-hydroxy-XDE-570	96-h LC_{50} > 100 mg a.i./L 96-h NOEC = 100 mg a.i./L	Practically non-toxic
	Chronic	Florasulam	28-d LC_{50} > 119 mg a.i./L 28-d NOEC = 119 mg a.i./L	Practically non-toxic
Bluegill sunfish	Acute	Florasulam	96-h LC_{50} > 100 mg a.i./L 96-h NOEC = 100 mg a.i./L	Practically non-toxic
Freshwater alga	Acute	Florasulam	diatom cell count 5-d EC_{25} = 0.18 mg a.i./L 5-d EC_{50} = 0.97 mg a.i./L 5-d NOEC = 0.049 mg a.i./L	N/A

Organism	Exposure	Test substance	End point value	Degree of toxicity[a]
		EF-1343	green algae biomass 72-h EC_{50} = 3.45 µg a.i./L 72-h NOEC = 1.75 µg a.i./L	N/A
		5-hydroxy-XDE-570	green algae cell count 96-h EC_{25} = 11.59 mg a.i./L 96-h EC_{50} = 25.57 mg a.i./L 96-h NOEC = 6.64 mg a.i./L	N/A
Vascular plant	Dissolved	Florasulam	duckweed frond number 14-d EC_{25} = 0.57 µg a.i./L 14-d EC_{50} = 1.18 µg a.i./L 14-d NOEC = 0.62 µg a.i./L	N/A
Marine species				
Crustacean	Acute	Florasulam	grass shrimp 96-h LC_{50} > 130 mg a.i./L 96-h NOEC = 130 mg a.i./L	Practically non-toxic
Mollusk	Acute	Florasulam	oyster shell deposition 96-h LC_{50} > 125 mg a.i./L 96-h NOEC = 125 mg a.i./L	Practically non-toxic
Fish	Acute	Florasulam	silverside 96-h LC_{50} > 122 mg a.i./L 96-h NOEC = 122 mg a.i./L	Practically non-toxic
Marine alga	Acute	Florasulam	marine diatom 5-d EC_{25} = 32.4 mg a.i./L 5-d EC_{50} = 47.6 mg a.i./L 5-d NOEC = 22.8 mg a.i./L	N/A

[a] USEPA classification, where applicable

Table 17 Risk to terrestrial organisms

Organism	Exposure	End point value	EEC	MOS	Risk
Invertebrates					
Earthworm	Acute	14-d NOEC = 1300 mg a.i./kg soil	0.0022 mg a.i./kg soil	5.9×10^5	No risk
Bee	Contact	NOEC 112 kg a.i./ha	5 g a.i./ha	2.2×10^4	No risk
Birds					
Japanese quail	Acute oral	14-d NOEC = 175 mg a.i./kg bw	0.6 mg a.i./kg dw diet	1.2×10^2 d	No risk
	Dietary	8-d NOEC = 5000 mg a.i./kg diet	0.6 mg a.i./kg dw diet	8.3×10^3	No risk
Bobwhite quail	Reproduction	NOEC = 1500 mg a.i./kg diet	0.6 mg a.i./kg dw diet	2.5×10^3	No risk
Mammals					
Mouse	Acute	LD_{50} > 5000 mg a.i./kg bw	2.51 mg a.i./kg dw diet	> 9.2×10^3 d	No risk

Organism	Exposure	End point value	EEC	MOS	Risk
Rat	Dietary	NOAEL = 100 mg a.i./kg bw/d (1621 mg a.i./kg dw diet)	2.52 mg a.i./kg dw diet	6.4×10^2	No risk
	Reproduction	NOAEL = 100 mg a.i./kg bw/d = 1621 mg a.i./kg dw diet	2.52 mg a.i./kg dw diet	6.4×10^2	No risk
Vascular plants					
Vascular plant	Seedling emergence	EC_{25} = 4.3 g a.i./ha	5 g a.i./ha	8.6×10^{-1}	Moderate risk
	Vegetative vigour	EC_{25} = 0.02 g a.i./ha	5 g a.i./ha	4×10^{-3}	Very high risk

Table 18 Risk to aquatic organisms

Organism	Exposure	End point value	EEC	MOS	Risk
Freshwater species					
Daphnia magna	Acute	48-h NOEC = 174 mg a.i./L	0.001667 mg a.i./L	1.04×10^5	No risk
	Chronic	21-d NOEC = 38.9 mg a.i./L	0.001667 mg a.i./L	2.33×10^4	No risk
Rainbow trout	Acute	96-h NOEC = 100 mg a.i./L	0.001667 mg a.i./L	6.00×10^4	No risk
	Chronic	28-d NOEC = 119 mg a.i./L	0.001667 mg a.i./L	7.14×10^4	No risk
Bluegill sunfish	Acute	96-h NOEC = 100 mg a.i./L	0.001667 mg a.i./L	6.00×10^4	No risk
Freshwater alga	Acute	72-h NOEC = 1.75 µg a.i./L	0.001667 mg a.i./L	1.05×10^0	Low risk
Vascular plant	Dissolved	14-d NOEC = 0.62 µg a.i./L	0.001667 mg a.i./L	3.7×10^{-1}	Moderate risk
Marine species					
Crustacean	Acute	96-h NOEC = 130 mg a.i./L	0.001667 mg a.i./L	7.8×10^4	No risk
Mollusk	Acute	96-h NOEC = 125 mg a.i./L	0.001667 mg a.i./L	7.50×10^4	No risk
Fish	Acute	96-h NOEC = 122 mg a.i./L	0.001667 mg a.i./L	7.32×10^4	No risk
Marine alga	Acute	5-d NOEC = 22.8 mg a.i./L	0.001667 mg a.i./L	1.37×10^4	No risk

Table 19 Proposed herbicide tank-mixes with EF-1343 Suspension Concentrate Herbicide, plus surfactant in spring wheat, durum wheat, spring barley and oats

Annual grass herbicide tank-mix	PCP Act registration no.	Broadleaf herbicide application rate	
		Product (L/ha)	Active Ingredient (g a.i./ha)
MCPA ester (500 g/L)	Several	0.84	420
Curtail M Herbicide	22764	1.5	495

Annual grass herbicide tank-mix	PCP Act registration no.	Broadleaf herbicide application rate	
		Product (L/ha)	Active ingredient (g a.i./ha)
Assert 300 SC Herbicide	21032	1.6	500
Horizon 240 EC Herbicide	24067	0.23–0.29	56–70
Puma Super Herbicide	25511	1	92

Table 20 Proposed non-ionic surfactant tank-mix with EF-1343 Suspension Concentrate Herbicide and tank-mix partners

Product name	PCP Act registration no.	Recommended application rate
Agral 90	11809 or 24725	0.2% v/v
Score	12200	0.8–1.0% v/v

Table 21 Alternative post-emergent herbicides for broadleaf weed control in cereals

Technical grade active ingredient	End-use products	Herbicide classification	
		Group	Mode of action
Metsulfuron methyl	Ally Herbicide	2	ALS inhibitor
Imazamethabenz	Assert Herbicide	2	ALS inhibitor
Fluroxypyr	Starane (Attain concept)	4	Synthetic auxin
Dicamba	Banvel Herbicide	4	Synthetic auxin
Basagran	Bentazon Herbicide	6	Inhibitor of photosystem II Site A
Bromoxynil	Pardner Herbicide	6	Inhibitor of photosystem II Site A
Thifensulfuron methyl	Refine Herbicide	2	ALS inhibitor
Tribenuron methyl	Express Toss n' go	2	ALS inhibitor
Clopyralid	Lontrel Herbicide	4	Synthetic auxin
Linuron	Linuron 400 L	7	Inhibitor of photosystem II Site B
Mecoprop	Mecoprop amine 400	4	Synthetic auxin
MCPA	several	4	Synthetic auxin
2,4-D	several	4	Synthetic auxin
Triasulfuron methyl	Unity 75 WG (Unity concept)	2	ALS inhibitor

Organism	Exposure	End point value	EEC	MOS	Risk
Rat	Dietary	NOAEL = 100 mg a.i./kg bw/d (1621 mg a.i./kg dw diet)	2.52 mg a.i./kg dw diet	6.4×10^2	No risk
	Reproduction	NOAEL = 100 mg a.i./kg bw/d = 1621 mg a.i./kg dw diet	2.52 mg a.i./kg dw diet	6.4×10^2	No risk
Vascular plants					
Vascular plant	Seedling emergence	EC_{25} = 4.3 g a.i./ha	5 g a.i./ha	8.6×10^{-1}	Moderate risk
	Vegetative vigour	EC_{25} = 0.02 g a.i./ha	5 g a.i./ha	4×10^{-3}	Very high risk

Table 18 Risk to aquatic organisms

Organism	Exposure	End point value	EEC	MOS	Risk
Freshwater species					
Daphnia magna	Acute	48-h NOEC = 174 mg a.i./L	0.001667 mg a.i./L	1.04×10^5	No risk
	Chronic	21-d NOEC = 38.9 mg a.i./L	0.001667 mg a.i./L	2.33×10^4	No risk
Rainbow trout	Acute	96-h NOEC = 100 mg a.i./L	0.001667 mg a.i./L	6.00×10^4	No risk
	Chronic	28-d NOEC = 119 mg a.i./L	0.001667 mg a.i./L	7.14×10^4	No risk
Bluegill sunfish	Acute	96-h NOEC = 100 mg a.i./L	0.001667 mg a.i./L	6.00×10^4	No risk
Freshwater alga	Acute	72-h NOEC = 1.75 µg a.i./L	0.001667 mg a.i./L	1.05×10^0	Low risk
Vascular plant	Dissolved	14-d NOEC = 0.62 µg a.i./L	0.001667 mg a.i./L	3.7×10^{-1}	Moderate risk
Marine species					
Crustacean	Acute	96-h NOEC = 130 mg a.i./L	0.001667 mg a.i./L	7.8×10^4	No risk
Mollusk	Acute	96-h NOEC = 125 mg a.i./L	0.001667 mg a.i./L	7.50×10^4	No risk
Fish	Acute	96-h NOEC = 122 mg a.i./L	0.001667 mg a.i./L	7.32×10^4	No risk
Marine alga	Acute	5-d NOEC = 22.8 mg a.i./L	0.001667 mg a.i./L	1.37×10^4	No risk

Table 19 Proposed herbicide tank-mixes with EF-1343 Suspension Concentrate Herbicide, plus surfactant in spring wheat, durum wheat, spring barley and oats

Annual grass herbicide tank-mix	PCP Act registration no.	Broadleaf herbicide application rate	
		Product (L/ha)	Active ingredient (g a.i./ha)
MCPA ester (500 g/L)	Several	0.84	420
Curtail M Herbicide	22764	1.5	495

Annual grass herbicide tank-mix	PCP Act registration no.	Broadleaf herbicide application rate	
		Product (L/ha)	Active ingredient (g a.i./ha)
Assert 300 SC Herbicide	21032	1.6	500
Horizon 240 EC Herbicide	24067	0.23–0.29	56–70
Puma Super Herbicide	25511	1	92

Table 20 Proposed non-ionic surfactant tank-mix with EF-1343 Suspension Concentrate Herbicide and tank-mix partners

Product name	PCP Act registration no.	Recommended application rate
Agral 90	11809 or 24725	0.2% v/v
Score	12200	0.8–1.0% v/v

Table 21 Alternative post-emergent herbicides for broadleaf weed control in cereals

Technical grade active ingredient	End-use products	Herbicide classification	
		Group	Mode of action
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Imazamethabenz	Assert Herbicide	2	ALS inhibitor
Fluroxypyr	Starane (Attain concept)	4	Synthetic auxin
Dicamba	Banvel Herbicide	4	Synthetic auxin
Basagran	Bentazon Herbicide	6	Inhibitor of photosystem II Site A
Bromoxynil	Pardner Herbicide	6	Inhibitor of photosystem II Site A
Thifensulfuron methyl	Refine Herbicide	2	ALS inhibitor
Tribenuron methyl	Express Toss n' go	2	ALS inhibitor
Clopyralid	Lontrel Herbicide	4	Synthetic auxin
Linuron	Linuron 400 L	7	Inhibitor of photosystem II Site B
Mecoprop	Mecoprop amine 400	4	Synthetic auxin
MCPA	several	4	Synthetic auxin
2,4-D	several	4	Synthetic auxin
Triasulfuron methyl	Unity 75 WG (Unity concept)	2	ALS inhibitor

Table 22 Summary of label proposals and recommendations based on value review

Proposed		Recommendation (based on value assessment)	Comments
Application timing	Cereals from the 2-leaf growth stage up to and including the flag leaf extended stage	Cereals from the 2- to 6-leaf stage	Majority of crop tolerance trials were conducted at the 2- to 6-leaf stage of cereals.
No. of applications	1 per year	same	
Application method	Ground application only DO NOT APPLY BY AIR. Do not apply through any type of irrigation system.	same	
Crops	Spring wheat	Yes	Adequate crop tolerance demonstrated with EF-1343 applied alone or in tank-mixes
	Durum wheat	Yes	Adequate crop tolerance demonstrated with EF-343 applied alone or in tank-mixes
	Spring barley	Yes	Adequate crop tolerance demonstrated with EF-1343 applied alone or in tank-mixes
	Oats (tank-mix only)	Yes	Adequate crop tolerance demonstrated with EF-1343 applied in tank-mixes
Weeds	Control of: volunteer canola (including Roundup Ready and Liberty Link), common chickweed, cleavers, shepherd's purse, smartweed, stinkweed, wild buckwheat, wild mustard	Yes	Adequate efficacy demonstrated with EF-1343 alone on requested weed species
	Suppression of: hempnettle, redroot pigweed, annual sowthistle, perennial sowthistle	Yes	Same with label statement for perennial sowthistle indicating that applications made at advanced leaf stages will reduce product effectiveness
Spray volume	50–100 L/ha	minimum of 100 L/ha	No data submitted for 50 L/ha for EF-1343 applied alone. Limited data submitted for MCPA ester tank-mix and Curtail tank-mix, which was not summarized in a manner to facilitate review

Proposed		Recommendation (based on value assessment)	Comments
Herbicide tank-mixes			
MCPA ester	Control of: volunteer canola (including Roundup Ready, Liberty Link, Smart), common chickweed, cleavers, dandelion (seedlings), flixweed, hempnettle, lamb's quarters, ball mustard, wild mustard, redroot pigweed, common ragweed, shepherd's purse, smartweed, stinkweed, stork's bill, wild buckwheat	Remove flixweed, move dandelion (seedlings) to suppression, move stork's bill to suppression	Sufficient data to demonstrate efficacy for the tank-mix with slight changes to the label: insufficient data for flixweed, dandelion seedlings suppression, stork's bill suppression
	Suppression of: Canada thistle (top growth only), dandelion (overwintered rosettes <15 cm), round-leaved mallow, annual sowthistle, perennial sowthistle (top growth control)	Remove round-leaved mallow	Insufficient data for round-leaved mallow
Curtail M	Control of: Canada thistle, volunteer canola (including Roundup Ready, Liberty Link, Smart), common chickweed, cleavers, dandelion (seedling, overwintered rosettes <15 cm), hempnettle, lamb's quarters, ball mustard, redroot pigweed, shepherd's purse, smartweed, annual sowthistle, perennial sowthistle, stinkweed, stork's bill, wild buckwheat, flixweed	Remove ball mustard, move perennial sowthistle to suppression, move dandelion to suppression, indicate flixweed (spring rosettes only)	Insufficient data for ball mustard, suppression for dandelion and perennial sowthistle, flixweed (spring rosettes only) per wording on the Curtail M label
	Suppression of: dandelion (overwintered rosettes >15 cm; mature plants), round-leaved mallow	Remove round-leaved mallow. Accept dandelion (seedlings and overwintered rosettes)	Insufficient data for round-leaved mallow Data for dandelion suggest wording as: seedlings and overwintered rosettes.
MCPA ester or Curtail M +Assert	Wild oats	Yes	Sufficient data
MCPA ester or Curtail M + Horizon	Wild oats, green foxtail	Yes	Same
MCPA ester or Curtail M + Puma Super	Wild oats	Yes	Same

Table 22 Summary of label proposals and recommendations based on value review

Proposed		Recommendation (based on value assessment)	Comments
Application timing	Cereals from the 2-leaf growth stage up to and including the flag leaf extended stage	Cereals from the 2- to 6-leaf stage	Majority of crop tolerance trials were conducted at the 2- to 6-leaf stage of cereals.
No. of applications	1 per year	same	
Application method	Ground application only DO NOT APPLY BY AIR. Do not apply through any type of irrigation system.	same	
Crops	Spring wheat	Yes	Adequate crop tolerance demonstrated with EF-1343 applied alone or in tank-mixes
	Durum wheat	Yes	Adequate crop tolerance demonstrated with EF-343 applied alone or in tank-mixes
	Spring barley	Yes	Adequate crop tolerance demonstrated with EF-1343 applied alone or in tank-mixes
	Oats (tank-mix only)	Yes	Adequate crop tolerance demonstrated with EF-1343 applied in tank-mixes
Weeds	Control of: volunteer canola (including Roundup Ready and Liberty Link), common chickweed, cleavers, shepherd's purse, smartweed, stinkweed, wild buckwheat, wild mustard	Yes	Adequate efficacy demonstrated with EF-1343 alone on requested weed species
	Suppression of: hempnettle, redroot pigweed, annual sowthistle, perennial sowthistle	Yes	Same with label statement for perennial sowthistle indicating that applications made at advanced leaf stages will reduce product effectiveness
Spray volume	50–100 L/ha	minimum of 100 L/ha	No data submitted for 50 L/ha for EF-1343 applied alone. Limited data submitted for MCPA ester tank-mix and Curtail tank-mix, which was not summarized in a manner to facilitate review

Proposed		Recommendation (based on value assessment)	Comments
Herbicide tank-mixes			
MCPA ester	Control of: volunteer canola (including Roundup Ready, Liberty Link, Smart), common chickweed, cleavers, dandelion (seedlings), flixweed, hempnettle, lamb's quarters, ball mustard, wild mustard, redroot pigweed, common ragweed, shepherd's purse, smartweed, stinkweed, stork's bill, wild buckwheat	Remove flixweed, move dandelion (seedlings) to suppression, move stork's bill to suppression	Sufficient data to demonstrate efficacy for the tank-mix with slight changes to the label: insufficient data for flixweed, dandelion seedlings suppression, stork's bill suppression
	Suppression of: Canada thistle (top growth only), dandelion (overwintered rosettes <15 cm), round-leaved mallow, annual sowthistle, perennial sowthistle (top growth control)	Remove round-leaved mallow	Insufficient data for round-leaved mallow
Curtail M	Control of: Canada thistle, volunteer canola (including Roundup Ready, Liberty Link, Smart); common chickweed, cleavers, dandelion (seedling, overwintered rosettes <15 cm), hempnettle, lamb's quarters, ball mustard, redroot pigweed, shepherd's purse, smartweed, annual sowthistle, perennial sowthistle, stinkweed, stork's bill, wild buckwheat, flixweed	Remove ball mustard, move perennial sowthistle to suppression, move dandelion to suppression, indicate flixweed (spring rosettes only)	Insufficient data for ball mustard, suppression for dandelion and perennial sowthistle, flixweed (spring rosettes only) per wording on the Curtail M label
	Suppression of: dandelion (overwintered rosettes >15 cm; mature plants), round-leaved mallow	Remove round-leaved mallow. Accept dandelion (seedlings and overwintered rosettes)	Insufficient data for round-leaved mallow Data for dandelion suggest wording as: seedlings and overwintered rosettes.
MCPA ester or Curtail M +Assert	Wild oats	Yes	Sufficient data
MCPA ester or Curtail M + Horizon	Wild oats, green foxtail	Yes	Same
MCPA ester or Curtail M + Puma Super	Wild oats	Yes	Same

Proposed		Recommendation (based on value assessment)	Comments
Rotational crops (re-crop the year following EF-1343 application)			
1	Barley	Yes	Rationale and plantback data acceptable
2	Canola	Yes	Recrop data acceptable
3	Forage grasses	No	Insufficient data or rationale not acceptable
4	Oats	No	Insufficient data or rationale not acceptable
5	Peas	Yes	Recrop data acceptable
6	Rye	No	Insufficient data or rationale not acceptable
7	Wheat	Yes	Rationale and plantback data acceptable
8	Summer fallow	Yes	Acceptable

Proposed		**Recommendation (based on value assessment)**	**Comments**
Rotational crops (re-crop the year following EF-1343 application)			
1	Barley	Yes	Rationale and plantback data acceptable
2	Canola	Yes	Recrop data acceptable
3	Forage grasses	No	Insufficient data or rationale not acceptable
4	Oats	No	Insufficient data or rationale not acceptable
5	Peas	Yes	Recrop data acceptable
6	Rye	No	Insufficient data or rationale not acceptable
7	Wheat	Yes	Rationale and plantback data acceptable
8	Summer fallow	Yes	Acceptable

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